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1,3-DINITROBENZENE, AND TETRYL IN RATS

SUBTITLE: 90 Day Toxicity Evaluation of 1,3-Dinitrobenzene (DNB)  
in Fischer 344 Rats

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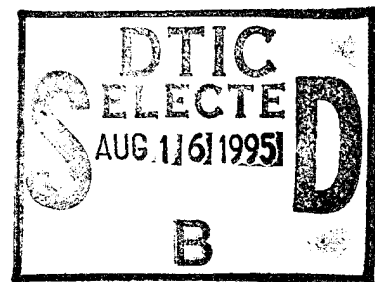
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Study Initiation: August 9, 1994

Initiation of Dosing: August 22 and 23, 1994


Completion of Necropsy: November 22 and 23, 1994

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## QUALITY ASSURANCE STATEMENT

The portions of this toxicology project performed and reported by Pathology Associates, Inc. has been inspected and audited by the quality assurance unit as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Environmental Protection Agency. The following table is a record of the inspections/audits performed and reported by the QAU.

<u>Date of Inspection</u>	<u>Phase Inspected</u>	<u>Date Findings Reported to Management and Study Director</u>
07-20-95	Final Report	07-20-95
02-06-95	Draft Report	02-06-95
02-06-95	Data	02-06-95
01-31-95	Draft Report	01-31-95
01-31-95	Data	01-31-95
12-09-94	Quality Control	12-09-94
11-28-94	Trimming	11-28-94
11-22-94	Necropsy	11-23-94
09-13-94	Food/Water Consumption	09-14-94
09-13-94	Weighing	09-13-94

  
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Date

Study Number: 94-004

## Compliance Statement

This study was conducted in compliance with the Good Laboratory Practice Regulations as set forth in Title 21 of the U.S. Code of Federal Regulations Part 792 issued August 17, 1989. All deviations from the protocol and/or GLPs are listed in Appendix J. There were no deviations from the aforementioned regulations which affected the quality or integrity of the study or the interpretation of the results in the report.

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## INTRODUCTION

Nitroaromatics, such as 1,3-dinitrobenzene (DNB), 1,3,5-trinitrobenzene (TNB), and N-methyl-N,2,4,6-tetranitroaniline (tetryl), have been detected as environmental contaminants of groundwater and soil near production sites and in some instances at military test grounds. DNB is formed as a by-product during 2,4,6-trinitrotoluene (TNT) production. It is also formed through photochemical oxidative degradation of 2,4-dinitrotoluene a by-product released into the environment from TNT manufacturing (Spanggord et.al., 1980). DNB and TNB are not easily biodegradable, persist in the environment, eventually leach out, and contaminate groundwater near waste disposal sites. Tetryl is an explosive that has been in use, largely for military purposes, since 1906. Wastewaters and soil at the original production sites and other plants devoted to munitions assembly, contain large quantities of these compounds (Walsh and Jenkins, 1992).

Toxicity data on these compounds are limited. The oral LD<sub>50</sub> of DNB, TNB and tetryl were 59 mg/kg, 284 mg/kg and greater than 5 g/kg, respectively, in rats for combined sexes. TNB and tetryl were not toxic at 2 g/kg when applied to rabbit skin for 24 hours. However, the dermal LD<sub>50</sub> of DNB was 1.99 g/kg for combined sexes of rabbits. None of these compounds produced skin irritation but positive (DNB) and severe (TNB, tetryl) eye irritation potentials in rabbits were noted. The sensitization tests showed that DNB and tetryl are not skin sensitizers while TNB caused mild allergic reaction in guinea pigs (Fitzgerald et. al., 1992 a,b,c). Some of the toxicological effects of DNB are: formation of methemoglobin, testicular degeneration and reproductive failure, weight loss and anemia in hamsters, rats and mice. Neurological and hematological disorders have also been reported in dogs. DNB is toxic to humans; the estimated lethal dose range is 5-50 mg/kg. It is readily absorbed through the skin (Von Burg, 1989). Tetryl was observed to be a powerful skin sensitizer in ammunition plant workers. Dermatitis, liver atrophy, spleen effects, headaches, weight loss and respiratory irritation were reported following tetryl exposure (U.S. EPA, 1990). Atmospheric concentration of 1.5 mg/m<sup>3</sup> or below did not produce systemic poisoning in persons working with tetryl. DNB, TNB and tetryl have been shown to be genotoxic in the Salmonella mutagenesis assay (McGregor et. al., 1989). TNB and DNB have been shown to form adducts of blood proteins and tissue DNA in rats (Reddy et. al.; 1991, 1995).

### Objective of the Study

This study was conducted in order to evaluate the toxicity of DNB when administered in the diet for 90 days.

## MATERIALS AND METHODS

### Test Material Preparation

1,3-Dinitrobenzene powder (CAS #99-65-0) was prepared by Fluka Chemical Corp. (Ronkonkoma, New York). The purity (99.15%) was confirmed by the U.S. EPA, Cincinnati. Certified powdered Purina Laboratory Chow 5002 was purchased (Ralston-Purina Co., St. Louis, MO) and stored at 4°C until used. DNB diets were prepared weekly. First, 45 mg of DNB was added to 25 g of powdered diet in a mortar and thoroughly ground with a pestle. Afterwards, the remaining diet 1475 g was added and mixed for 120 minutes in a mechanical mixer (Kitchen Aid, St. Joseph, MI) for uniform distribution of DNB in the diet. This was verified by determining the DNB concentration in the diet, taken from each of the 1 kg mixtures, by quantitative analysis done by HPLC. The premixed diet (30 mg/kg) was further diluted with fresh powdered diet to obtain the desired DNB concentration in the lower dose groups. The diet feeders were refilled twice a week and changed weekly.

Analyses of the DNB-feed mixtures were carried out on acetone extracts of the mixtures, utilizing a Waters 600E chromatography system (Waters, Milford, MA), equipped with a 490E programmable multiwavelength detector, operating at 230 nm. The entire chromatography system was interfaced with a Berthold HPLC computer program, Version 1.65 (Berthold, Nashua, NH). The DNB was eluted from a Zorbax C-8 column (9.4 mm x 25 cm) (MAC-DOD Analytical, Chadds Ford, PA) with a water-methanol gradient, at a flow rate of 3 ml/min. The gradient had an initial condition of 20% methanol which was increased in a linear fashion from 20% to 50% in 15 minutes and then to 65% in 25 minutes, and finally to 100% in 10 minutes. The column was washed for an additional 5 minutes and brought back to 20% methanol by reverse gradient and equilibrated for an additional 10 minutes at initial conditions before the next sample was injected. Working standards were prepared in Burdick and Jackson HPLC grade high purity methanol (Baxter, Obetz, OH). Analytical data of these mixtures is present in Appendix I.

### Animals and Maintenance

Male and female Fischer 344 rats, confirmed free of viral antibodies, bacteria and parasites, were obtained from Charles River Laboratories, Kingston, New York. The animals, 6 weeks old and weighing approximately 120-125 g when delivered, were held for 2 weeks in quarantine prior to initiation of treatment. The animals were housed in a temperature (20-22°C) and humidity (40-60%) controlled room on a 12:12 hour light:dark cycle. For the study, they were housed individually in polycarbonate cages and water was administered ad libitum. Animal identification was done using electronic implants (Bio Medic, Maywood, NJ) with the rats assigned to control and treatment groups according to a computer-generated set of random numbers. The weight variation of the animals of each sex used did not exceed  $\pm 2$  s.d. of the mean weight at the time of delivery. The cages were identified with a color-coded identification card indicating the animal and treatment group. All aspects of the study were conducted in compliance with the guidelines of the American Association for Accreditation of Laboratory Animal Care.



All rats were observed twice daily for physiological and behavioral responses as well as for mortality or morbidity. Food and water consumption were recorded twice weekly. Body weights were taken prior to the start of the study, once weekly during the study and at the final sacrifice.

#### Experiment Design

Group	No. of Animals	Sex	Diet Concentration (mg DNB/kg diet)
1	15	F	30
2	15	F	6
3	15	F	1
4	15	F	0
5	15	M	30
6	15	M	6
7	15	M	1
8	15	M	0

#### Hematology and Clinical Chemistry

Hematology and clinical chemistry analyses were carried out at 45 days (5 rats/group) and at 90 days (10 rats/group).

Hematology parameters were assessed using a Serono-Baker Hematology Analyzer, Model 9000. Total red and white blood cell counts, platelet count, reticulocyte count, differential leukocyte count, hemoglobin and packed cell volume were measured and computed. Methemoglobin samples were analyzed on a IL 482 Co-Oximeter. Heinz bodies were determined using the crystal violet procedure (Lee et. al., 1993) with microscopic examination for positive cells (>5 Heinz bodies).

Clinical chemistry was performed using a COBAS Fara II centrifugal analyzer (Roche, Nutley, NJ) with a non-selective electrode (ISE) module. Clinical chemistry analytes included sodium, potassium, total protein, albumin, calcium, phosphorus, total bilirubin, blood urea nitrogen, creatinine, alanine aminotransferase, cholesterol, triglycerides, aspartate aminotransferase, glucose and alkaline phosphatase.

#### Statistical Evaluation

Males and females were considered separately in all statistical analyses. A one-factor (dose) analysis of variance (ANOVA) was used to analyze normally distributed measures: body weights, organ weights, organ weight ratios, food and water consumption, hematology and clinical chemistry. When a treatment effect was noted ( $p \leq 0.05$ , F-test) the difference between the control and the treatment groups was probed using a multiple comparison procedure (Dunnett's t-test).

## Necropsy and Histopathology

Prior to necropsy, the animals were anesthetized with pentobarbital (60 mg/kg b.w., i. p.) and blood samples were collected via cardiac puncture after the body weight was recorded. Following euthanasia via exsanguination, all external surfaces, orifices, external surface of the brain, cervical tissues, all organs, and the thoracic, abdominal and pelvic cavities were examined for gross lesions.

During necropsy the following tissues were weighed: brain, liver, spleen, kidneys, adrenals, lungs, thymus, testes w/epididymides, ovaries, and heart.

The following tissues were harvested from each animal and preserved in 10% neutral buffered formalin:

skin	colon
mandibular and	cecum
mesenteric lymph nodes	rectum
mammary glands	liver
thigh muscle	pancreas
sciatic nerve	spleen
sternum with marrow	kidneys
femur with marrow	adrenals
thymus	urinary bladder
trachea	seminal vesicles
lungs with bronchi	prostate
heart and aorta	testes, including epididymides
thyroid	ovaries
parathyroids	uterus
esophagus	nasal cavity with turbinates
stomach	brain
duodenum	pituitary
jejunum	preputial or clitoral glands
tongue	Zymbal's gland
salivary gland	thoracic spinal cord
ileum	eyes
harderian gland	

Subsequently, these tissues were trimmed, processed and embedded in paraffin. Blocks were sectioned at 5 $\mu$  and slides were prepared and stained with hematoxylin and eosin. All tissues were examined in the high dose and control groups of both sexes. The spleen of both sexes and the testes and kidneys of males were identified as target organs and examined in the appropriate groups.

The inflammatory and degenerative lesions were graded according to severity using a scale of one to four (minimal, mild, moderate or marked). Data were tabulated according to individual animal and summarized by group. In addition, the gross observations and microscopic diagnoses were correlated for each animal. Labcat histopathology software was used for data management.

### Specimen, Raw data, and Final Report Storage

All tissue specimens, blocks and slides, raw data and final report will be placed in the U.S. EPA storage facility.

## RESULTS

### Food and Water Consumption

Food and water consumption data are listed in Table 1, while individual data are presented in Appendix A. There were no significant differences amongst groups for either food or water consumption.

Using the food consumption data, the average daily DNB dose levels received by group (see Experimental Design) are presented in Table 2. The average daily DNB doses consumed (mg/kg b.w.) were, 0.07, 0.39 and 1.93 for females and 0.06, 0.35 and 1.73 for males.

### Body Weights, Organ Weights and Weight Ratios

The mean group values for body weights are listed in Table 3, while mean group organ weights (heart, brain, spleen, adrenals, thymus, ovaries/testes, kidneys, lungs and liver) are given in Table 4. Mean group values for organ to body weight ratios and terminal body weights are present in Table 5. Individual body weights are found in Appendix B with individual organ weights present in Appendix C.

No significant changes from control terminal body weights were noted in any of the treated groups.

Organ weights as a percent of the total body weight were significantly ( $p \leq 0.05$ ) different from controls for the following organs:

- Spleen - The 30 mg DNB dose group of both sexes had increased values.
- Testes - The male 30 mg DNB dose group had a decreased value.

### Hematology

Hematology analyses performed were total white blood cell count (WBC), platelet count, red blood count (RBC), methemoglobin, hemoglobin (HGB), hematocrit (HCT), reticulocytes, Heinz bodies and differential leukocyte count. Group data for 45 and 90 days are summarized in Tables 6-9. Individual data are listed in Appendix D.

#### 1. WBC and Differential:

There were no significant differences in total white cell count or differentials amongst the groups in either sex at 45 or 90 days.

2. RBC:

A significant decrease ( $p \leq 0.05$ ) in red blood cell count was present in both sexes receiving 30 mg DNB diet at 45 and 90 days.

3. Hemoglobin:

A significant decrease ( $p \leq 0.05$ ) was noted in hemoglobin levels in both sexes in the 30 mg DNB dose group at both 45 days and 90 days. Hemoglobin was also decreased in the 6 mg DNB male group at 90 days.

4. Hematocrit:

A significant decrease ( $p \leq 0.05$ ) was present in both sexes in the 30 mg DNB dose group at 45 and 90 days.

5. Platelets:

There were no significant changes in total platelets in any treatment group at 45 days but at 90 days the 30 mg DNB female group was significantly increased.

6. Reticulocytes:

A significant increase ( $p \leq 0.05$ ) was noted in both sexes in the 30 mg DNB dose group at 45 and 90 days. A significant increase was also noted in the male 6 mg DNB dose group at 45 days.

7. Methemoglobin:

A significant increase ( $p \leq 0.05$ ) was present in both sexes receiving 30 and 6 mg DNB diet at 45 and 90 days except for males in the 6 mg dose group at 45 days.

8. Heinz Bodies:

Heinz bodies were not evident in any treatment group.

### Clinical Chemistry

The mean group values for each analyte are compiled in Tables 10-13. Individual data are present in Appendix E.

1. Total Protein:

There were no significant differences amongst the groups at either 45 or 90 days except for a slight increase in the male 6 mg DNB dose group at 45 days.

2. Albumin:

There were no significant differences amongst the groups at either 45 or 90 days except for a slight increase in the male 6 mg DNB dose group at 45 days.

3. Calcium:

A significant increase ( $p \leq 0.05$ ) was present in females receiving 30 mg DNB diet for 45 days while a decrease was noted in males receiving 30 mg DNB for 90 days.

4. Total Bilirubin:

There were no significant differences amongst the groups in either sex at 45 or 90 days.

5. Blood Urea Nitrogen (BUN):

A significant increase ( $p \leq 0.05$ ) was noted in males receiving 6 and 1 mg DNB diet for 45 days while a decrease was evident in males receiving 30 and 6 mg DNB for 90 days.

6. Creatinine:

A significant increase ( $p \leq 0.05$ ) was present in males receiving 6 mg DNB diet for 45 days.

7. Aspartate Aminotransferase (AST):

There were no significant differences amongst the groups in either sex at 45 or 90 days.

8. Alanine Aminotransferase (ALT):

There were no significant differences amongst the groups in either sex at 45 or 90 days.

9. Alkaline Phosphatase (ALK Phos):

A significant decrease ( $p \leq 0.05$ ) was noted in males receiving 30 mg DNB diet for 90 days.

10. Sodium:

There were no significant differences amongst the groups in either sex at 45 or 90 days.

11. Potassium:

There were no significant differences amongst the groups in either sex at 45 or 90 days.

12. Glucose:

A significant increase ( $p \leq 0.05$ ) was noted in females receiving 1 mg DNB diet for 45 days.

13. Phosphorus:

There were no significant differences amongst the groups in either sex at 45 or 90 days.

14. Cholesterol:

A significant decrease ( $p \leq 0.05$ ) was noted in females receiving 1 mg DNB diet for 45 days.

15. Triglycerides:

There were no significant differences amongst the groups in either sex at 45 or 90 days.

Clinical Observations

Clinical observations are listed in Appendix F. There were no clinical observations that were meaningful.

Ophthalmology Data (Appendix G)

All animals used in this study were affected with mild corneal dystrophy prior to the initiation of the study. Corneal dystrophy is a common finding in Fischer 344 rats of both sexes. Progression of the corneal dystrophy was not observed to occur and the dystrophy did not interfere with ophthalmic examination in this study. Conjunctivitis was observed in a single animal and is unassociated with treatment. There was no treatment-related ophthalmic effect observed in the animals on this study.

Mortality

There were no early deaths in any of the groups.

Gross Pathology

Treatment related gross changes noted at the terminal sacrifice were confined to the male 30 mg DNB dose group. This change was a prominent decrease in testicular size.

## Histopathology (Appendix H)

All tissues were histopathologically examined in control and high dose animals of both sexes while the spleen, testes and kidneys were examined in all the appropriate remaining dose groups.

Significant changes were confined to the high dose (30 mg DNB/kg diet) group of both sexes involving the spleen and kidneys while testicular changes were noted in high dose males. The spleen was characterized by a minimal to mild erythroid cell hyperplasia and pigment deposition (hemosiderin). Only the spleen was examined in all the animals even though this same compensatory change can be noted in multiple organs. Regenerative anemia, as noted by the hematology results was the probable initiating factor for this response. The kidneys exhibited an increased deposition of cytoplasmic droplets in renal cortical tubular epithelial cells. These droplets were morphologically similar to the hyaline droplets noted in the 14 day DNB study except for a diminished intensity of eosinophilic staining in males while those noted in females were yellow-brown in color. The severity of this change was minimal to mild in the high dose groups only. The droplets stained positive with Mallory's Heidenhain protein stain. In addition to the deposition of hyaline droplets, the presence of early chronic progressive nephropathy was evident in both treated as well as control male rats. This change was characterized by an increased incidence of tubular degeneration and regeneration as well as mineralized foci.

The testes were characterized by severe seminiferous tubular degeneration. The affected tubules were lined by fewer spermatogenic cells and contained a reduced number of mature spermatides. Cell debris and some multinucleated cells were also present in the tubules as well as in the ducts of the epididymis. The diameter of the affected tubules was decreased with the interstitium being more condensed and prominent. The remaining diagnoses were considered spontaneous since their incidence levels were significantly low.

## SUMMARY

The administration to Fischer 344 rats of 1,3-dinitrobenzene at various doses in the diet for ninety days resulted in the following significant findings:

1. Relative and absolute spleen weights were increased in both sexes in the 30 mg DNB dose groups while testicular weights were decreased in the male 30 mg group.
2. A significant decrease in red blood cell count, hemoglobin and hematocrit levels were apparent in both sexes receiving 30 mg DNB diet while reticulocyte levels were increased in these same groups. Methemoglobin levels were increased in both sexes receiving 30 and 6 mg DNB diet.
3. Microscopic examination revealed significant changes in the testes (seminiferous tubular degeneration) in males, spleen (erythroid cell hyperplasia) and kidneys (cytoplasmic droplet deposition) of male and female animals receiving 30 mg DNB/kg diet.

4. A LOAEL of 0.35 mg DNB/kg b.w./day based on hematological effects and a NOAEL of 0.060 mg DNB/kg b.w./day has been established.

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Table 1: Food and Water Consumption

Dose	Food	Water
(mg DNB/kg diet)	(g/kg b.w./day)	(g/kg b.w./day)
Females		
30	65.45 ± 0.68	103.79 ± 2.88
6	65.27 ± 0.56	102.82 ± 3.68
1	66.46 ± 0.76	95.03 ± 1.92
0	66.29 ± 0.66	102.42 ± 3.33
Males		
30	58.51 ± 0.25	72.50 ± 1.32
6	59.29 ± 0.34	77.22 ± 1.17
1	59.40 ± 0.31	76.12 ± 1.14
0	59.68 ± 0.55	76.71 ± 0.88
Mean ± Standard Error		

Table 2: Calculated Daily DNB Consumption

Dose (mg DNB/kg diet)	Calculated Dose (mg DNB/kg b.w.)	
	Females	Males
30	1.93 ± 0.02	1.73 ± 0.01
6	0.39 ± 0.00	0.35 ± 0.00
1	0.07 ± 0.00	0.06 ± 0.00
0	0.00 ± 0.00	0.00 ± 0.00

Mean ± Standard Error

Table 3: Body Weights (grams)

Weeks	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
Females				
1	140.24±1.16	141.34±1.64	141.15±1.83	139.71±0.97
2	147.27±1.79	149.18±1.74	150.06±2.28	147.51±0.85
3	155.74±2.10	156.12±1.86	157.57±2.52	156.59±0.97
4	159.51±2.51	159.93±1.79	160.57±2.58	158.90±1.24
5	164.19±2.32	164.54±2.23	166.04±2.48	163.93±1.33
6	169.59±2.89	168.70±2.27	172.51±2.97	169.03±1.60
7	173.88±2.87	175.38±2.51	177.10±3.04	173.71±1.82
8	176.80±3.13	177.82±2.74	179.67±3.25	174.75±2.03
9	177.45±3.11	176.50±2.56	180.23±3.29	176.00±1.89
10	179.49±3.38	179.57±3.00	183.22±3.59	175.80±1.82
11	180.75±3.26	181.83±2.78	184.81±3.44	178.81±2.21
12	186.48±3.59	187.50±3.28	189.15±3.51	185.69±2.51
13	182.64±3.41	183.34±2.86	187.08±3.54	181.88±2.56
Males				
1	190.63±2.77	194.88±2.66	191.35±1.71	192.90±2.32
2	211.80±3.56	216.82±2.83	211.91±1.78	216.34±2.47
3	234.12±4.30	241.58±2.86	236.41±1.83	238.81±2.53
4	247.30±4.86	258.41±3.52	252.49±2.34	256.49±2.62
5	260.55±5.47	274.97±3.95	267.70±2.76	270.95±3.23
6	273.20±6.02	292.58±4.18	281.71±3.43	287.17±3.88
7	287.54±7.10	307.91±4.90	295.59±4.22	301.13±4.31
8	293.22±6.53	313.06±5.74	298.37±3.72	305.01±4.41
9	296.02±7.00	316.19±5.64	301.87±4.28	306.82±5.92
10	300.94±7.31	322.98±6.30	310.30±3.83	313.28±6.09
11	306.14±8.09	329.92±6.62	317.46±5.00	317.89±7.24
12	316.51±7.94	338.31±7.22	326.65±4.69	327.56±8.47
13	315.58±8.28	337.12±7.48	326.16±4.80	324.90±8.49
Mean ± Standard Error				

Table 4: Organ Weights (grams)

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
Females				
Kidneys	1.23±0.03	1.18±0.02	1.18±0.02	1.17±0.02
Liver	4.66±0.10	4.58±0.08	4.59±0.11	4.53±0.10
Brain	1.76±0.02	1.78±0.01	1.75±0.01	1.74±0.01
Spleen	0.52±0.02 *	0.43±0.01	0.42±0.01	0.45±0.01
Adrenals	0.06±0.00	0.06±0.00	0.06±0.00	0.07±0.00
Thymus	0.20±0.01	0.21±0.01	0.20±0.01	0.20±0.01
Lung	0.93±0.03	0.96±0.03	0.92±0.02	0.97±0.03
Ovaries	0.12±0.01	0.14±0.01	0.14±0.01	0.14±0.01
Heart	0.68±0.02	0.64±0.02	0.67±0.02	0.64±0.01
Males				
Kidneys	2.03±0.06	2.25±0.06	2.16±0.05	2.10±0.06
Liver	8.43±0.36	9.00±0.26	8.84±0.24	8.74±0.35
Brain	1.87±0.03	1.87±0.02	1.92±0.01	1.92±0.01
Spleen	0.73±0.02 *	0.66±0.02	0.60±0.01	0.62±0.02
Adrenals	0.05±0.00	0.07±0.01	0.05±0.01	0.06±0.00
Thymus	0.26±0.02	0.28±0.03	0.29±0.02	0.25±0.01
Testes	2.90±0.22 *	5.84±0.33 *	4.82±0.27	4.73±0.34
Heart	0.92±0.03	1.05±0.03	0.98±0.02	0.96±0.03
Lung	1.29±0.03	1.48±0.04	1.30±0.04	1.37±0.06

Mean ± Standard Error

\* Significantly different from the control group ( $p \leq 0.05$ ) by Dunnett's test.

Table 5: Organ-to-Body Weight Ratios

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
Females				
Body Weight(g)	176.33±3.30	174.47±2.69	177.43±3.18	172.48±2.23
Kidneys (%)	0.70±0.01	0.67±0.01	0.67±0.01	0.68±0.01
Lung (%)	0.53±0.02	0.55±0.02	0.52±0.01	0.56±0.01
Liver (%)	2.65±0.04	2.63±0.03	2.59±0.05	2.63±0.04
Heart (%)	0.39±0.01	0.37±0.01	0.38±0.01	0.37±0.01
Brain (%)	1.00±0.02	1.02±0.02	0.99±0.01	1.01±0.01
Spleen (%)	0.30±0.01 *	0.25±0.00	0.24±0.00	0.26±0.01
Adrenals (%)	0.03±0.00	0.04±0.00	0.03±0.00	0.04±0.00
Thymus (%)	0.11±0.01	0.12±0.01	0.11±0.01	0.12±0.00
Ovaries (%)	0.07±0.00	0.08±0.00	0.08±0.01	0.08±0.01
Males				
Body Weight(g)	302.73±8.12	322.34±7.25	314.22±4.55	310.58±8.08
Kidneys (%)	0.67±0.01	0.70±0.01	0.69±0.01	0.68±0.01
Lung (%)	0.43±0.01	0.46±0.01	0.41±0.01	0.44±0.01
Liver (%)	2.78±0.06	2.79±0.03	2.81±0.04	2.81±0.05
Heart (%)	0.30±0.00	0.33±0.01	0.31±0.00	0.31±0.01
Brain (%)	0.62±0.01	0.58±0.01	0.61±0.01	0.62±0.01
Spleen (%)	0.24±0.00 *	0.21±0.00	0.19±0.00	0.20±0.01
Adrenals (%)	0.02±0.00	0.02±0.00	0.02±0.00	0.02±0.00
Thymus (%)	0.09±0.01	0.09±0.01	0.09±0.01	0.08±0.00
Testes (%)	0.97±0.09 *	1.81±0.09	1.54±0.09	1.51±0.08
Mean ± Standard Error				

\* Significantly different from the control group ( $p \leq 0.05$ ) by Dunnett's test.

Table 6: Hematology Values/Females  
45 Days

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
RBC ( $\times 10^6/\mu\text{l}$ )	7.38 * $\pm 0.09$	8.06 $\pm 0.17$	7.92 $\pm 0.17$	8.10 $\pm 0.20$
Hemoglobin (g/dl)	13.96 * $\pm 0.15$	15.06 $\pm 0.40$	14.78 $\pm 0.33$	15.06 $\pm 0.31$
Hematocrit (%)	40.28 * $\pm 0.58$	42.34 $\pm 1.25$	41.68 $\pm 1.43$	42.42 $\pm 0.99$
WBC ( $\times 10^3/\mu\text{l}$ )	3.90 $\pm 0.57$	3.46 $\pm 0.57$	3.04 $\pm 0.52$	3.14 $\pm 0.45$
Platelets ( $\times 10^3/\mu\text{l}$ )	814.00 $\pm 46.45$	777.80 $\pm 11.95$	779.80 $\pm 30.59$	759.00 $\pm 44.03$
Neutrophils (%)	15.68 $\pm 4.34$	18.74 $\pm 4.10$	18.96 $\pm 5.43$	18.48 $\pm 1.49$
Lymphocytes (%)	80.56 $\pm 5.42$	78.28 $\pm 3.63$	77.32 $\pm 5.41$	77.90 $\pm 1.24$
MCV (cubic $\mu\text{m}$ )	54.60 * $\pm 0.66$	52.54 $\pm 0.50$	52.66 $\pm 0.78$	52.36 $\pm 0.44$
MCH (picogram)	18.92 * $\pm 0.08$	18.68 $\pm 0.15$	18.68 $\pm 0.11$	18.58 $\pm 0.08$
MCHC (g/dl)	34.68 * $\pm 0.35$	35.56 $\pm 0.26$	35.44 $\pm 0.59$	35.48 $\pm 0.16$
Reticulocytes (%)	4.60 * $\pm 0.41$	2.56 $\pm 0.13$	2.34 $\pm 0.32$	2.14 $\pm 0.50$
MetHb (%)	4.06 * $\pm 0.59$	1.50 * $\pm 0.10$	0.70 $\pm 0.32$	0.66 $\pm 0.42$

Mean  $\pm$  Standard Deviation

\* Significantly different from the control group ( $P \leq 0.05$ ) by the Dunnett's test.

Table 7: Hematology Values/Males  
45 Days

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
RBC ( $\times 10^6/\mu\text{l}$ )	8.24 * $\pm 0.13$	8.95 $\pm 0.22$	8.94 $\pm 0.14$	8.98 $\pm 0.11$
Hemoglobin (g/dl)	14.24 * $\pm 0.22$	15.08 $\pm 0.43$	15.22 $\pm 0.26$	15.26 $\pm 0.24$
Hematocrit (%)	42.36 * $\pm 0.82$	44.44 $\pm 1.12$	44.44 $\pm 0.99$	44.32 $\pm 0.43$
WBC ( $\times 10^3/\mu\text{l}$ )	4.50 $\pm 0.99$	4.44 $\pm 0.96$	4.04 $\pm 0.83$	4.12 $\pm 0.90$
Platelets ( $\times 10^3/\mu\text{L}$ )	701.40 $\pm 108.6$	751.00 $\pm 64.82$	777.60 $\pm 78.51$	761.40 $\pm 22.59$
Neutrophils (%)	18.66 $\pm 1.95$	23.16 $\pm 4.30$	22.32 $\pm 2.37$	23.70 $\pm 3.79$
Lymphocytes (%)	78.24 $\pm 2.18$	73.56 $\pm 4.70$	74.50 $\pm 2.65$	72.76 $\pm 3.84$
MCV (cubic $\mu\text{m}$ )	51.42 $\pm 0.38$	43.66 $\pm 13.45$	49.70 $\pm 0.63$	49.34 $\pm 0.43$
MCH (picogram)	17.26 * $\pm 0.05$	16.86 $\pm 0.13$	17.04 $\pm 0.21$	16.98 $\pm 0.08$
MCHC (g/dl)	33.58 * $\pm 0.31$	33.90 $\pm 0.33$	34.28 $\pm 0.36$	34.44 $\pm 0.38$
Reticulocytes (%)	4.50 * $\pm 0.40$	3.20 * $\pm 0.25$	2.82 $\pm 0.51$	2.50 $\pm 0.19$
MethHb (%)	4.44 * $\pm 1.00$	1.30 $\pm 0.66$	0.78 $\pm 0.42$	0.58 $\pm 0.26$

Mean  $\pm$  Standard Deviation

\* Significantly different from the control group ( $P \leq 0.05$ ) by the Dunnett's test.

Table 8: Hematology Values/Females  
90 Days

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
RBC (x10 <sup>6</sup> /μl)	7.33 * ±0.19	7.81 ±0.19	8.02 ±0.15	7.91 ±0.17
Hemoglobin (g/dl)	14.21 * ±0.30	15.13 ±0.29	15.44 ±0.13	15.33 ±0.35
Hematocrit (%)	39.61 * ±1.43	40.88 ±1.11	41.96 ±1.11	41.45 ±0.72
WBC (x10 <sup>3</sup> /μl)	3.72 ±0.61	3.03 ±0.73	3.03 ±0.70	3.47 ±0.67
Platelets (x10 <sup>3</sup> /μl)	697.40 * ±26.79	648.10 ±44.17	626.40 ±40.84	642.30 ±39.61
Neutrophils (%)	17.29 ±6.61	19.87 ±5.22	20.62 ±6.37	19.41 ±4.27
Lymphocytes (%)	75.65 ±5.56	76.37 ±5.98	72.84 ±7.16	77.37 ±4.80
MCV (cubic μm)	54.03 * ±0.87	52.31 ±0.31	52.27 ±0.53	52.36 ±0.70
MCH (picogram)	19.40 ±0.19	19.37 ±0.16	19.33 ±0.32	19.36 ±0.20
MCHC (g/dl)	35.79 * ±0.68	36.97 ±0.39	36.98 ±0.94	36.96 ±0.49
Reticulocytes (%)	3.56 * ±0.57	1.92 ±0.15	1.83 ±0.19	1.74 ±0.35
MetHb (%)	3.77 * ±0.23	1.59 * ±0.27	1.11 ±0.50	0.72 ±0.40

Mean ± Standard Deviation

\* Significantly different from the control group (P ≤ 0.05) by the Dunnett's test.



Table 9: Hematology Values/Males  
90 Days

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
RBC (x10 <sup>6</sup> /μl)	8.14 * ±0.16	8.93 ±0.24	9.00 ±0.26	8.99 ±0.20
Hemoglobin (g/dl)	14.48 * ±0.21	15.31 * ±0.32	15.56 ±0.30	15.64 ±0.25
Hematocrit (%)	41.25 * ±0.80	43.13 ±1.54	43.94 ±1.11	44.10 ±0.89
WBC (x10 <sup>3</sup> /μl)	4.26 ±1.13	3.55 ±1.01	3.49 ±0.56	4.12 ±0.93
Platelets (x10 <sup>3</sup> /μL)	659.60 ±46.47	635.33 ±48.83	606.11 ±48.84	675.00 ±142.5
Neutrophils (%)	19.94 ±3.91	20.53 ±3.97	21.03 ±3.44	20.88 ±3.03
Lymphocytes (%)	77.13 ±4.07	75.33 ±3.62	75.48 ±3.92	75.64 ±3.25
MCV (cubic μm)	50.68 * ±0.67	48.31 * ±0.64	48.81 ±0.47	49.06 ±0.67
MCH (picogram)	17.79 * ±0.26	17.15 ±0.21	17.27 ±0.29	17.41 ±0.26
MCHC (g/dl)	35.09 ±0.41	35.50 ±0.73	35.40 ±0.42	35.47 ±0.53
Reticulocytes (%)	3.15 * ±0.50	1.95 ±0.40	1.73 ±0.15	1.73 ±0.34
MetHb (%)	4.11 * ±0.45	1.46 * ±0.43	0.78 ±0.35	0.75 ±0.14

Mean ± Standard Deviation

\* Significantly different from the control group ( $P \leq 0.05$ ) by the Dunnett's test.

Table 10: Clinical Chemistry Values/Females  
45 Days

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
Glucose (mg/dl)	106.20 ± 8.93	117.60 ± 13.07	129.00 ± 22.99*	102.60 ± 12.20
BUN (mg/dl)	21.80 ± 2.59	22.80 ± 1.64	22.60 ± 2.30	20.00 ± 2.55
Creatinine (mg/dl)	0.58 ± 0.04	0.54 ± 0.05	0.50 ± 0.00	0.56 ± 0.05
ALK Phos. (U/L)	105.40 ± 11.24	114.80 ± 11.67	108.20 ± 7.22	105.00 ± 14.70
AST (U/L)	156.60 ± 40.43	159.20 ± 47.61	138.60 ± 35.87	146.00 ± 23.38
ALT (U/L)	56.40 ± 21.92	68.80 ± 25.05	56.00 ± 15.54	49.40 ± 17.01
Potassium (mmol/L)	4.38 ± 0.28	4.36 ± 0.32	4.70 ± 0.65	4.32 ± 0.18
Albumin (g/dl)	4.62 ± 0.13	4.62 ± 0.08	4.36 ± 0.18	4.46 ± 0.13
Calcium (mg/dl)	10.18 ± 0.08*	9.98 ± 0.13	9.86 ± 0.23	9.92 ± 0.15
Sodium (mmol/dl)	140.00 ± 0.71	140.80 ± 0.84	140.60 ± 0.89	140.80 ± 0.45
Total Bilirubin (mg/dl)	0.14 ± 0.05	0.16 ± 0.09	0.16 ± 0.05	0.16 ± 0.05
Total Protein (g/dl)	6.02 ± 0.13	6.06 ± 0.11	5.74 ± 0.19	5.90 ± 0.19
Cholesterol (mg/dl)	94.00 ± 3.39	90.80 ± 4.60	79.80 ± 2.86*	89.00 ± 5.24
Phosphorus (mg/dl)	9.06 ± 0.89	7.86 ± 1.07	8.20 ± 1.31	8.60 ± 0.86
Triglyceride (mg/dl)	33.80 ± 4.66	33.80 ± 3.96	28.00 ± 3.54	29.80 ± 3.56

Mean ± Standard Deviation

\*Significantly different from the control group ( $p \leq 0.05$ ) by the Dunnett's test.

Table 11: Clinical Chemistry Values/Males  
45 Days

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
Glucose (mg/dl)	168.20 ± 10.96	177.80 ± 16.02	173.00 ± 10.27	159.80 ± 18.70
BUN (mg/dl)	19.80 ± 1.10	20.80 ± 1.64*	20.20 ± 1.30*	17.60 ± 1.52
Creatinine (mg/dl)	0.56 ± 0.05	0.58 ± 0.04*	0.56 ± 0.05	0.50 ± 0.00
ALK Phos. (U/L)	117.00 ± 8.86	128.00 ± 7.84	129.20 ± 6.06	115.20 ± 8.90
AST (U/L)	227.60 ± 126.94	205.60 ± 92.62	157.80 ± 18.57	159.60 ± 30.93
ALT (U/L)	147.40 ± 143.04	126.20 ± 105.46	69.20 ± 10.83	81.00 ± 24.11
Potassium (mmol/L)	4.72 ± 0.13	5.08 ± 0.33	5.12 ± 0.36	5.12 ± 0.23
Albumin (g/dl)	4.64 ± 0.11	4.78 ± 0.08*	4.54 ± 0.09	4.50 ± 0.07
Calcium (mg/dl)	10.36 ± 0.17	10.52 ± 0.15	10.40 ± 0.24	10.40 ± 0.10
Sodium (mmol/dl)	140.80 ± 0.45	142.40 ± 5.41	140.20 ± 0.84	139.60 ± 0.55
Total Bilirubin (mg/dl)	0.10 ± 0.00	0.12 ± 0.04	0.10 ± 0.00	0.10 ± 0.00
Total Protein (g/dl)	6.32 ± 0.13	6.56 ± 0.26*	6.18 ± 0.24	6.22 ± 0.11
Cholesterol (mg/dl)	57.60 ± 5.94	57.00 ± 3.46	53.20 ± 4.02	54.00 ± 2.65
Phosphorus (mg/dl)	9.36 ± 0.31	9.42 ± 0.52	9.78 ± 0.67	9.68 ± 0.31
Triglyceride (mg/dl)	81.60 ± 38.60	105.80 ± 28.67	95.80 ± 28.27	75.20 ± 15.29

Mean ± Standard Deviation

\*Significantly different from the control group (p≤0.05) by the Dunnett's test.

Table 12: Clinical Chemistry Values/Females  
90 Days

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
Glucose (mg/dl)	111.00 ± 10.38	108.40 ± 9.37	115.10 ± 9.79	118.70 ± 12.37
BUN (mg/dl)	19.40 ± 1.71	17.60 ± 1.65	17.90 ± 1.91	17.80 ± 1.81
Creatinine (mg/dl)	0.58 ± 0.08	0.57 ± 0.05	0.60 ± 0.05	0.59 ± 0.06
ALK Phos. (U/L)	80.00 ± 13.11	73.10 ± 17.65	78.50 ± 13.28	78.70 ± 9.92
AST (U/L)	157.00 ± 26.89	165.00 ± 25.25	157.80 ± 34.42	149.90 ± 33.37
ALT (U/L)	67.00 ± 16.04	64.00 ± 14.62	76.40 ± 31.10	65.40 ± 17.61
Potassium (mmol/L)	4.18 ± 0.38	4.06 ± 0.28	4.27 ± 0.31	4.29 ± 0.39
Albumin (g/dl)	4.51 ± 0.23	4.34 ± 0.15	4.43 ± 0.30	4.38 ± 0.18
Calcium (mg/dl)	9.90 ± 0.25	9.85 ± 0.22	9.86 ± 0.16	9.83 ± 0.14
Sodium (mmol/dl)	143.56 ± 1.13	143.40 ± 1.26	143.20 ± 0.79	143.10 ± 1.20
Total Bilirubin (mg/dl)	0.16 ± 0.13	0.11 ± 0.03	0.12 ± 0.04	0.10 ± 0.00
Total Protein (g/dl)	6.30 ± 0.36	6.12 ± 0.20	6.25 ± 0.42	6.20 ± 0.29
Cholesterol (mg/dl)	107.80 ± 20.24	108.00 ± 6.39	106.40 ± 9.35	102.80 ± 9.45
Phosphorus (mg/dl)	8.70 ± 0.67	7.70 ± 1.23	7.71 ± 1.17	7.96 ± 1.10
Triglyceride (mg/dl)	33.22 ± 8.44	35.60 ± 6.93	34.80 ± 6.97	31.10 ± 4.70

Mean ± Standard Deviation

Table 13: Clinical Chemistry Values/Males  
90 Days

	Dose Groups (mg DNB/kg diet)			
	30	6	1	0
Glucose (mg/dl)	164.60 ± 16.80	149.80 ± 11.13	154.10 ± 15.01	155.20 ± 19.99
BUN (mg/dl)	18.30 ± 2.16*	18.90 ± 2.92*	20.90 ± 2.08	21.70 ± 2.50
Creatinine (mg/dl)	0.62 ± 0.04	0.61 ± 0.06	0.60 ± 0.05	0.62 ± 0.04
ALK Phos. (U/L)	86.70 ± 11.67*	90.20 ± 14.47	104.20 ± 11.47	102.40 ± 13.18
AST (U/L)	214.90 ± 78.29	218.90 ± 51.60	220.10 ± 27.41	235.50 ± 49.49
ALT (U/L)	116.20 ± 48.81	106.80 ± 30.43	107.80 ± 23.67	126.10 ± 45.11
Potassium (mmol/L)	4.43 ± 0.41	4.61 ± 0.33	4.41 ± 0.25	4.58 ± 0.37
Albumin (g/dl)	4.52 ± 0.18	4.46 ± 0.14	4.59 ± 0.14	4.58 ± 0.14
Calcium (mg/dl)	10.01 ± 0.15*	10.20 ± 0.19	10.22 ± 0.20	10.22 ± 0.20
Sodium (mmol/dl)	143.00 ± 0.82	143.10 ± 1.10	143.00 ± 0.82	143.80 ± 0.92
Total Bilirubin (mg/dl)	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.00	0.09 ± 0.03
Total Protein (g/dl)	6.32 ± 0.22	6.48 ± 0.20	6.56 ± 0.22	6.55 ± 0.20
Cholesterol (mg/dl)	73.60 ± 8.02	79.60 ± 8.73	76.20 ± 10.14	81.60 ± 12.19
Phosphorus (mg/dl)	8.26 ± 0.56	8.33 ± 0.54	7.97 ± 0.47	8.34 ± 0.51
Triglyceride (mg/dl)	59.80 ± 29.36	69.20 ± 27.03	88.10 ± 34.17	79.50 ± 21.57

Mean ± Standard Deviation

\*Significantly different from the control group ( $p \leq 0.05$ ) by the Dunnett's test.

APPENDIX A

FOOD AND WATER  
CONSUMPTION

# Individual Food and Water Consumption

## Females

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 1	Week 2	Week 3	Week 4	Week 5	Week 1	Week 2	Week 3	Week 4	Week 5
30	1	78.5	79.6	84.6	88.1	84.9	119.4	124.1	115.4	130.7	134.9
	2	71.3	120.5	122.2	104.7	73.7	111.0	138.3	151.2	212.2	181.5
	3	81.7	89.5	119.5	98.2	93.5	126.9	171.3	160.4	225.7	171.5
	4	70.9	93.7	99.1	135.8	98.6	115.4	181.0	176.0	251.2	187.6
	5	74.1	70.3	99.5	89.6	95.1	127.2	150.5	154.1	224.8	181.5
	6	71.3	30.6	68.5	110.8	101.5	117.0	282.8	230.6	235.2	188.9
	7	79.0	112.9	99.4	109.3	92.4	125.7	145.4	142.3	205.1	166.4
	8	77.5	88.1	121.9	100.6	111.1	126.0	163.0	153.3	217.5	188.2
	9	73.7	91.8	120.0	74.6	113.3	126.4	185.6	194.4	260.2	210.1
	10	75.6	92.1	80.8	76.6	89.3	114.7	190.1	191.4	240.1	186.4
6	11	82.3	140.5	111.7	90.0	115.4	115.3	192.8	202.4	252.1	216.3
	12	83.8	112.5	120.2	113.3	105.4	116.6	145.1	182.9	243.7	184.9
	13	76.1	97.1	100.8	74.7	88.5	125.6	143.1	143.8	229.0	212.1
	14	80.9	111.6	122.2	100.2	93.0	122.4	216.1	242.9	262.4	232.3
	15	69.9	104.2	100.8	83.0	119.4	116.5	168.5	186.6	227.1	192.8
	16	73.3	126.9	79.6	79.6	98.1	95.1	172.7	173.0	212.9	177.1
	17	76.9	93.3	89.0	137.8	108.7	129.8	187.7	174.8	239.7	198.0
	18	72.5	99.9	118.8	84.9	83.6	130.9	191.3	201.5	259.6	228.5
	19	74.9	112.8	102.2	97.3	95.7	107.0	119.3	136.0	195.7	179.6
	20	85.9	87.1	84.3	93.4	132.8	103.1	143.7	156.9	168.9	160.6

# Individual Food and Water Consumption

## Females

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 6	Week 7	Week 8	Week 9	Week 10	Week 6	Week 7	Week 8	Week 9	Week 10
30	1	33.3	63.9	65.0	59.5	98.2	58.1	96.4	114.7	95.5	143.2
	2	72.6	128.0	107.5	74.3	144.0	126.5	174.1	176.1	173.8	249.4
	3	83.5	59.5	104.4	76.4	98.1	135.2	155.1	178.3	171.2	244.1
	4	98.8	112.5	61.4	84.6	114.9	164.7	187.3	198.1	189.8	253.8
	5	80.2	152.8	131.7	97.8	117.9	129.7	173.7	173.9	166.7	255.5
	6	92.4	105.3	80.9	56.9	103.9	147.3	170.6	186.4	191.5	250.0
	7	100.3	100.6	98.9	52.4	65.2	124.3	159.0	150.4	159.9	187.8
	8	94.7	114.4	171.5	69.2	116.9	133.3	132.1	181.6	154.7	215.5
	9	116.6	107.9	70.3	81.4	147.5	161.3	153.8	201.0	207.0	254.2
	10	109.9	108.7	78.4	82.4	114.0	162.7	126.2	161.1	187.2	234.7
6	11	103.5	149.8	98.3	79.4	139.8	183.9	179.9	166.0	179.8	239.1
	12	93.4	99.9	131.4	97.4	133.4	163.3	164.2	203.0	191.8	257.8
	13	89.6	81.9	111.1	119.7	103.9	141.1	152.8	136.8	168.9	213.1
	14	97.7	71.6	88.3	98.0	74.7	154.6	190.4	246.5	207.1	267.6
	15	120.6	78.9	64.9	89.4	91.3	135.6	131.0	162.7	169.6	191.7
	16	44.6	100.5	87.3	81.8	153.2	153.4	119.8	168.3	181.0	215.1
	17	107.4	128.0	109.3	104.8	127.8	163.6	143.5	165.9	169.5	232.8
	18	83.7	132.3	89.4	102.2	121.0	184.9	180.2	213.4	207.4	244.8
	19	76.0	141.5	76.2	61.8	86.3	135.9	138.4	129.5	148.1	194.4
	20	75.1	100.6	105.8	54.3	83.7	130.0	85.4	136.5	126.9	169.5



# Individual Food and Water Consumption

## Females

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)			Water (g/wk)		
		Week 11	Week 12	Week 13*	Week 11	Week 12	Week 13*
30	1	38.9	63.5	37.4	62.3	108.8	63.0
	2	68.1	113.5	34.3	152.0	181.8	47.9
	3	63.0	99.6	32.2	149.8	176.2	51.5
	4	55.9	79.7	32.8	185.2	196.5	49.2
	5	81.7	77.1	36.4	182.1	175.2	50.8
	6	106.1	94.5	32.6	181.5	207.3	57.2
	7	91.6	74.8	36.8	138.7	188.1	51.7
	8	119.1	137.8	39.5	134.2	180.9	53.5
	9	96.3	111.9	37.8	171.1	211.5	55.4
	10	100.4	75.3	35.7	156.2	168.3	44.7
6	11	91.8	172.2	34.4	166.4	186.8	51.3
	12	60.5	92.9	31.2	171.4	184.8	49.1
	13	45.0	128.5	34.3	123.2	191.3	50.6
	14	35.7	120.7	39.4	149.7	244.6	66.7
	15	87.5	67.3	30.6	110.8	157.9	48.1
	16	103.6	108.4	31.3	136.8	155.6	48.0
	17	92.6	124.2	31.3	139.2	188.9	48.7
	18	89.7	115.8	33.8	152.1	219.1	60.5
	19	75.9	85.1	32.5	114.7	177.8	49.8
	20	75.2	121.1	30.4	101.8	146.7	34.0

\*Week 13 is only 5 days

# Individual Food and Water Consumption

## Females

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 1	Week 2	Week 3	Week 4	Week 5	Week 1	Week 2	Week 3	Week 4	Week 5
1	21	82.8	117.0	98.2	120.0	141.3	136.3	160.9	155.1	194.1	195.6
	22	77.6	95.7	78.1	94.3	100.7	125.7	160.1	173.7	197.6	187.0
	23	81.5	120.4	94.5	94.4	102.6	123.1	170.0	168.6	193.2	174.9
	24	81.8	104.9	108.8	79.3	96.9	126.2	186.0	187.4	214.7	203.3
	25	82.8	116.1	127.8	83.9	90.2	117.8	163.2	127.1	165.9	167.5
	26	85.5	132.8	118.3	107.1	84.9	125.0	156.3	132.5	212.6	237.9
	27	77.3	97.7	82.1	85.6	78.1	108.7	138.1	120.8	189.9	212.9
	28	76.8	108.5	101.6	105.4	110.6	117.3	179.9	164.1	211.1	230.0
	29	75.0	74.0	111.8	77.3	86.0	111.5	151.3	124.5	160.6	209.8
	30	76.0	127.3	67.1	91.6	96.5	90.6	121.5	104.4	155.7	192.1
0	31	75.9	117.0	100.9	86.3	111.6	108.2	130.4	127.3	170.6	206.2
	32	72.0	100.3	74.8	100.0	100.0	123.3	173.6	160.6	200.8	229.7
	33	73.6	97.5	71.5	91.8	105.4	131.7	202.6	171.5	241.4	241.8
	34	72.2	143.4	92.6	92.4	94.2	131.4	215.0	153.4	207.9	231.9
	35	76.9	107.6	106.7	104.8	90.0	115.6	163.1	135.3	163.1	194.7
	36	63.5	84.0	118.8	76.8	73.9	126.1	182.4	155.8	201.4	225.3
	37	75.6	85.4	93.4	80.3	124.3	97.7	129.8	121.4	151.9	143.3
	38	77.5	101.9	131.6	81.0	112.3	110.6	162.8	167.1	218.9	223.0
	39	72.3	103.9	102.9	81.4	118.4	124.5	191.9	161.8	221.1	244.4
	40	74.2	89.5	71.7	102.5	69.4	104.3	169.8	127.5	175.7	194.4

# Individual Food and Water Consumption

## Females

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 6	Week 7	Week 8	Week 9	Week 10	Week 6	Week 7	Week 8	Week 9	Week 10
1	21	120.6	104.3	155.2	113.8	139.5	148.6	124.9	162.1	159.4	183.1
	22	121.5	85.1	94.9	74.0	94.9	140.4	114.6	161.6	145.2	189.1
	23	104.1	105.6	118.8	103.5	161.5	126.2	118.5	153.8	141.9	179.5
	24	145.5	120.8	111.4	101.3	151.3	167.3	140.2	197.6	167.3	208.2
	25	95.4	116.9	105.2	89.1	111.3	108.9	140.2	130.5	152.7	203.8
	26	84.9	113.9	67.9	53.6	100.3	128.6	190.8	175.2	176.3	236.8
	27	79.4	104.8	93.3	87.2	132.9	99.2	178.2	153.2	164.7	223.9
	28	97.1	81.2	106.4	73.6	81.0	120.7	210.0	185.3	190.9	264.9
	29	87.6	80.6	88.5	90.0	92.2	81.1	171.3	122.6	152.6	215.1
	30	87.9	51.6	65.4	147.3	124.1	92.4	165.1	139.3	159.8	205.2
0	31	99.5	119.2	104.3	79.4	104.3	79.0	198.2	158.2	171.6	254.0
	32	78.6	85.1	102.1	54.3	104.8	98.7	198.6	182.0	182.3	253.8
	33	107.3	84.0	89.6	93.2	123.5	134.6	216.0	193.4	190.6	258.5
	34	121.9	77.9	91.9	68.7	84.9	123.5	231.3	196.8	212.3	275.0
	35	106.6	99.5	100.2	101.2	99.5	87.5	224.6	174.1	180.3	278.4
	36	105.6	64.0	93.5	107.1	89.7	112.3	207.3	173.8	212.4	239.5
	37	176.1	81.9	98.2	74.7	107.0	41.9	157.5	99.6	151.2	211.6
	38	120.4	103.7	97.2	83.9	88.2	104.7	168.4	158.4	170.0	203.3
	39	103.8	86.3	88.8	85.0	120.5	128.4	198.0	180.1	189.5	248.8
	40	96.1	65.3	85.2	97.6	75.3	96.9	160.6	134.1	138.0	167.2

# Individual Food and Water Consumption

## Females

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)			Water (g/wk)		
		Week 11	Week 12	Week 13*	Week 11	Week 12	Week 13*
1	21	90.4	157.6	36.3	107.8	191.2	65.6
	22	58.4	77.7	32.5	117.9	175.7	49.9
	23	110.8	89.2	34.5	98.5	157.9	48.1
	24	139.3	152.8	35.0	128.4	184.8	50.8
	25	69.4	116.8	30.7	123.2	165.6	47.1
	26	47.2	75.0	29.9	150.8	190.0	49.1
	27	108.0	113.5	46.8	155.1	179.9	49.3
	28	78.8	104.5	30.5	180.2	219.6	52.0
	29	50.2	86.4	32.0	142.0	164.5	44.8
	30	82.1	89.3	31.5	145.4	164.6	41.9
0	31	52.6	159.2	31.6	163.1	198.4	49.1
	32	84.3	60.0	34.5	193.5	204.4	57.9
	33	114.8	160.7	33.7	193.7	204.6	57.7
	34	86.6	112.2	30.5	204.5	217.3	64.4
	35	70.0	132.7	35.8	166.4	185.8	50.3
	36	93.5	98.9	32.0	187.7	199.2	59.6
	37	87.1	140.8	37.1	141.9	183.1	48.8
	38	63.5	84.9	35.1	141.7	173.6	49.0
	39	99.3	104.6	34.5	163.6	211.0	59.7
	40	94.9	72.0	27.8	146.0	138.3	37.6

\*Week 13 is only 5 days

# Individual Food and Water Consumption

## Males

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 1	Week 2	Week 3	Week 4	Week 5	Week 1	Week 2	Week 3	Week 4	Week 5
30	41	94.8	114.8	161.3	135.4	153.5	136.7	256.7	216.6	239.6	285.4
	42	94.6	109.6	161.6	155.1	149.1	119.2	219.4	200.1	225.6	242.9
	43	110.0	169.7	158.0	177.3	153.5	148.3	223.0	191.1	207.2	251.2
	44	104.0	169.7	183.3	188.9	159.3	126.0	227.1	215.1	231.8	253.0
	45	98.8	184.8	169.8	147.6	126.5	135.5	207.7	158.2	199.0	216.2
	46	97.3	185.3	177.8	157.8	149.6	124.6	190.1	158.4	197.5	208.8
	47	92.7	163.8	132.2	212.0	94.4	98.7	146.6	138.1	172.9	186.5
	48	94.0	162.8	158.8	165.9	151.1	130.9	220.5	190.5	249.4	244.6
	49	98.4	165.2	172.3	202.4	174.4	130.8	207.9	228.6	249.2	248.5
	50	83.2	138.8	138.6	130.9	153.3	110.1	170.4	193.9	168.4	227.1
6	51	110.7	201.4	170.5	190.3	211.6	146.4	232.8	254.2	218.6	279.3
	52	92.4	169.9	192.5	144.2	161.9	130.2	242.4	258.9	190.9	270.7
	53	97.8	170.9	168.6	156.6	166.6	138.3	226.3	235.6	173.3	264.3
	54	94.0	148.6	165.3	157.3	142.2	130.4	231.6	248.2	206.3	279.8
	55	98.7	180.0	191.2	147.0	154.5	139.1	216.9	239.3	250.1	273.2
	56	84.9	137.0	192.8	222.8	149.4	147.6	233.0	250.7	253.4	282.4
	57	109.2	117.0	160.9	138.4	143.6	153.2	241.2	229.2	221.1	247.2
	58	100.5	189.8	192.7	162.2	175.8	140.4	279.7	271.9	235.7	300.5
	59	100.3	178.3	175.7	177.8	182.8	130.5	212.4	216.2	180.4	248.7
	60	95.1	175.7	171.6	163.2	147.6	135.0	248.6	253.7	187.3	271.4

# Individual Food and Water Consumption

## Males

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 6	Week 7	Week 8	Week 9	Week 10	Week 6	Week 7	Week 8	Week 9	Week 10
30	41	136.2	146.0	153.3	130.4	184.2	146.9	232.1	215.2	207.0	270.2
	42	112.7	159.0	135.3	112.2	192.2	131.2	238.5	193.1	198.5	243.8
	43	127.7	207.3	104.7	99.4	216.9	95.5	196.9	151.6	163.0	247.1
	44	109.5	188.1	142.4	102.3	215.0	150.5	199.8	202.4	181.4	245.0
	45	97.9	190.5	131.2	106.9	168.2	106.5	175.4	172.2	144.0	212.8
	46	53.4	213.2	92.2	121.1	222.5	116.9	167.3	182.8	138.9	212.7
	47	64.0	140.1	100.3	132.3	165.2	104.2	144.6	160.6	141.2	216.7
	48	120.5	165.6	122.3	92.0	183.3	175.0	221.2	228.7	193.0	247.1
	49	139.4	183.1	178.8	139.1	224.7	151.3	190.6	209.2	170.0	260.7
	50	120.6	126.8	92.0	86.4	144.2	153.0	148.8	212.8	145.2	230.7
6	51	173.7	195.4	202.0	122.8	216.6	207.5	207.8	257.7	177.0	285.3
	52	149.4	171.9	158.7	144.9	213.9	210.6	216.1	289.6	216.6	347.0
	53	131.1	159.1	103.0	133.6	175.9	202.5	176.4	214.1	169.5	242.2
	54	142.5	187.6	184.0	100.6	223.7	203.1	189.2	258.5	190.4	303.2
	55	144.7	174.2	147.0	107.4	122.7	196.1	204.1	219.8	161.6	259.3
	56	125.5	172.1	144.8	145.6	183.5	186.0	218.2	300.8	194.6	301.8
	57	143.6	178.0	130.9	113.7	200.3	208.0	202.8	245.7	189.8	271.4
	58	145.7	182.9	143.7	125.6	187.7	218.0	210.0	265.6	208.4	287.5
	59	144.2	148.1	131.9	129.1	169.1	189.2	168.3	216.7	177.5	271.9
	60	121.8	172.1	148.4	112.3	133.1	199.6	188.3	258.0	191.4	289.4

# Individual Food and Water Consumption

## Males

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)			Water (g/wk)		
		Week 11	Week 12	Week 13*	Week 11	Week 12	Week 13*
30	41	112.9	153.8	49.3	187.8	214.2	59.4
	42	128.7	96.6	44.4	186.6	198.4	57.1
	43	152.1	141.4	54.0	163.8	214.0	61.7
	44	154.7	163.0	49.9	166.4	236.6	57.4
	45	83.1	76.4	47.8	124.1	169.3	53.6
	46	159.1	178.2	44.0	139.6	197.0	49.2
	47	107.7	133.1	44.2	126.0	186.6	50.4
	48	118.6	111.7	45.7	169.0	216.3	56.1
	49	148.8	149.6	56.8	156.3	203.0	58.0
	50	116.9	144.3	36.3	165.7	182.6	49.3
6	51	132.4	190.8	59.7	173.1	224.8	63.3
	52	105.7	206.9	54.1	222.7	255.6	66.1
	53	134.1	115.6	45.8	157.9	213.4	57.6
	54	171.6	191.7	52.4	191.1	226.2	63.5
	55	52.2	132.4	44.0	157.3	209.0	54.0
	56	157.7	148.5	49.1	180.0	229.5	64.8
	57	113.0	131.1	47.6	163.6	210.4	57.0
	58	96.6	133.3	45.8	185.3	204.7	54.7
	59	136.5	198.3	48.6	150.6	217.7	58.8
	60	75.5	134.3	49.5	179.0	217.5	57.8

\*Week 13 is only 5 days

# Individual Food and Water Consumption

## Males

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 1	Week 2	Week 3	Week 4	Week 5	Week 1	Week 2	Week 3	Week 4	Week 5
1	61	86.6	159.5	202.5	185.7	160.0	133.2	213.0	221.6	205.0	232.1
	62	99.5	177.6	191.3	159.3	160.5	129.7	212.5	191.6	223.0	238.2
	63	94.6	184.6	154.7	167.7	175.2	128.4	227.6	211.2	226.8	238.3
	64	88.7	150.9	170.2	164.5	170.0	137.1	246.4	222.2	223.6	259.0
	65	94.1	153.7	182.1	139.3	141.1	121.1	226.5	207.4	178.5	203.9
	66	89.2	175.1	186.4	178.6	171.9	124.2	242.1	259.0	221.8	279.5
	67	99.4	146.5	165.2	159.3	174.7	121.0	193.7	191.1	197.7	208.9
	68	91.0	193.6	187.1	180.5	199.5	126.0	201.0	178.4	225.3	228.5
	69	99.3	157.6	161.9	156.3	161.9	141.7	213.7	177.3	263.5	254.4
	70	83.2	179.1	152.0	204.4	164.5	136.8	230.8	196.6	262.4	266.7
0	71	102.7	131.6	158.5	181.5	167.4	126.4	211.5	190.0	256.9	257.4
	72	113.5	167.4	122.0	177.1	182.9	152.5	235.6	197.2	215.8	227.6
	73	99.2	160.1	189.1	142.8	114.6	119.2	196.0	188.8	187.5	234.7
	74	99.6	143.7	170.5	154.4	124.1	132.7	196.3	254.1	216.9	270.4
	75	101.5	173.7	196.0	133.6	154.2	126.9	184.6	243.7	246.8	256.3
	76	99.9	150.6	175.2	153.1	193.3	137.3	251.7	313.0	291.8	297.0
	77	99.9	170.6	173.4	146.8	185.9	150.0	216.3	262.4	268.4	284.6
	78	105.4	194.3	172.2	142.1	156.2	144.8	220.7	276.1	265.5	277.4
	79	89.0	138.5	184.1	165.4	115.4	126.1	180.1	254.1	248.2	252.0
	80	92.1	166.2	152.0	152.4	135.6	125.8	187.1	231.0	194.1	243.3



# Individual Food and Water Consumption

## Males

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 6	Week 7	Week 8	Week 9	Week 10	Week 6	Week 7	Week 8	Week 9	Week 10
1	61	107.6	138.7	141.8	117.1	172.8	167.1	197.2	228.2	173.4	291.8
	62	139.9	167.4	143.6	124.4	189.1	173.7	208.5	260.1	186.8	275.6
	63	149.0	136.6	131.7	94.9	172.4	182.4	206.7	269.4	203.9	273.6
	64	180.6	137.4	153.5	101.3	163.6	194.5	192.2	234.7	200.7	260.1
	65	128.6	155.3	117.6	76.1	153.5	168.0	169.3	189.2	181.5	229.2
	66	121.5	178.0	157.3	120.5	226.3	195.7	203.5	253.8	216.9	301.9
	67	133.1	121.2	115.4	119.6	176.5	165.3	161.3	169.1	156.2	238.5
	68	154.3	175.5	124.3	111.1	197.8	165.4	199.2	223.9	177.6	250.7
	69	124.5	169.4	149.4	97.2	156.0	151.4	121.8	231.8	161.0	241.7
	70	123.4	181.6	152.3	74.7	165.2	192.5	206.1	242.6	186.6	255.1
0	71	140.5	143.0	199.8	110.7	143.7	163.0	185.8	215.5	164.7	245.5
	72	184.4	171.1	157.7	130.0	175.5	194.8	173.4	245.7	179.6	245.7
	73	112.6	131.8	139.4	86.5	162.8	172.8	179.8	178.8	156.8	245.7
	74	170.5	147.8	160.5	108.3	178.1	181.8	210.3	232.0	174.8	286.0
	75	138.3	161.4	142.9	107.6	179.9	185.0	240.9	215.6	184.7	273.5
	76	172.2	232.9	146.7	133.4	212.1	200.8	281.3	250.8	225.9	335.1
	77	142.2	188.7	163.0	103.0	156.5	168.1	254.1	213.6	196.9	311.5
	78	159.0	176.2	186.2	102.5	206.9	193.3	253.1	245.1	215.5	303.9
	79	137.1	127.9	125.4	132.6	111.7	157.8	207.0	205.1	179.7	262.4
	80	182.6	157.3	126.5	84.4	139.6	167.1	199.7	216.7	163.5	260.3

# Individual Food and Water Consumption

## Males

Dose Group (mg DNB/kg diet)	Animal Number	Food (g/wk)			Water (g/wk)		
		Week 11	Week 12	Week 13*	Week 11	Week 12	Week 13*
1	61	121.5	177.7	60.1	151.7	219.5	67.2
	62	134.6	168.7	51.9	146.2	226.3	56.1
	63	139.2	150.8	52.3	158.5	244.1	67.0
	64	128.6	137.1	44.4	152.8	223.5	53.9
	65	95.6	141.9	50.4	127.5	211.4	55.2
	66	154.7	191.4	48.9	167.9	236.3	59.2
	67	111.3	179.6	50.2	134.5	224.8	55.7
	68	100.8	185.1	50.9	135.6	216.9	56.0
	69	123.6	134.9	46.4	138.9	216.2	51.3
	70	125.9	114.3	**	142.1	224.4	59.6
0	71	110.9	145.6	61.7	147.2	211.0	52.9
	72	111.7	160.5	56.4	144.6	229.0	66.3
	73	107.2	107.2	46.2	155.7	202.2	51.4
	74	165.2	119.3	59.7	180.7	228.6	61.7
	75	138.5	200.6	37.1	176.5	226.5	51.1
	76	161.6	198.5	58.2	216.2	247.0	65.3
	77	141.8	160.8	55.5	185.5	231.4	65.7
	78	126.4	172.2	50.9	193.0	221.7	60.1
	79	51.4	113.3	42.5	156.8	198.1	55.4
	80	122.4	177.7	44.8	163.4	197.8	54.2

\*Week 13 is only 5 days, \*\*Data Unavailable

APPENDIX B  
BODY WEIGHTS

# Weekly Body Weights (grams)/Females

Dose (mg DNB/kg diet)	Animal Number	Weeks							
		1	2	3	4	5	6	7	8
30	1	141.7	150.6	159.9	164.3	169.5	178.8	181.6	187.2
	2	145.4	153.4	162.2	166.3	170.2	176.7	180.7	186.1
	3	143.7	155.4	165.0	170.7	174.9	180.6	185.1	186.8
	4	136.7	138.7	149.1	149.3	156.0	160.7	162.7	165.8
	5	136.3	140.2	145.9	149.3	155.7	154.7	160.6	162.6
	6	144.4	147.2	154.8	156.1	161.4	169.9	170.6	175.7
	7	139.7	148.3	153.5	161.7	166.4	170.6	173.8	176.1
	8	140.7	149.7	160.8	162.4	165.1	172.6	179.6	181.8
	9	139.3	148.5	158.9	165.6	169.6	174.4	180.9	183.2
	10	134.5	140.7	147.3	149.4	153.1	156.9	163.2	162.7
6	11	148.1	157.7	165.9	169.5	175.7	178.0	185.8	189.2
	12	150.5	156.1	164.9	167.2	172.0	179.4	186.1	191.2
	13	145.0	152.7	158.6	161.6	171.0	172.2	178.1	180.6
	14	143.3	150.7	158.7	162.6	164.1	169.5	176.5	178.8
	15	135.6	139.8	148.9	151.4	152.4	156.1	161.9	164.7
	16	137.5	145.8	150.5	155.6	158.7	162.9	165.4	168.0
	17	140.8	149.8	155.4	161.0	167.6	172.6	181.0	182.7
	18	138.9	146.8	150.6	156.4	160.5	165.4	171.8	177.0
	19	136.7	143.5	153.0	154.5	160.7	163.2	172.1	170.0
	20	137.0	148.9	154.7	159.5	162.7	167.7	175.1	176.0
1	21	146.7	154.1	161.3	165.9	171.2	180.9	186.3	188.0
	22	147.3	159.0	165.5	166.1	169.0	179.0	183.6	182.2
	23	143.9	155.6	165.8	171.5	175.9	182.6	188.6	191.9
	24	143.2	152.0	159.0	162.2	171.3	179.3	182.8	187.5
	25	142.9	153.3	163.0	164.8	168.9	175.2	179.4	185.5
	26	144.8	156.1	164.6	168.0	172.5	176.8	180.9	184.8
	27	137.9	143.5	148.4	151.6	157.0	164.4	168.2	172.0
	28	142.1	149.0	155.7	156.9	165.1	171.3	175.9	178.2
	29	131.0	139.4	147.1	150.0	156.4	160.0	165.8	165.2
	30	131.7	138.6	145.3	148.7	153.1	155.6	159.5	161.4
0	31	143.4	150.4	159.3	164.7	169.6	175.0	178.5	182.5
	32	139.9	149.2	158.1	158.3	164.9	171.5	174.0	170.6
	33	140.2	148.7	156.5	158.0	165.3	172.7	178.5	178.1
	34	143.0	149.5	154.5	155.7	160.0	164.4	169.0	166.4
	35	136.6	143.5	152.8	159.9	157.9	162.9	168.1	173.7
	36	141.4	148.0	159.2	159.2	165.1	168.8	176.6	177.7
	37	142.1	147.5	159.6	160.9	167.6	172.6	179.1	180.7
	38	136.7	148.3	159.1	164.7	168.4	173.2	179.8	179.1
	39	139.8	148.1	156.1	155.0	162.6	169.4	170.5	176.1
	40	134.0	141.9	150.7	152.6	157.9	159.8	163.0	162.6

# Weekly Body Weights (grams)/Females

Dose (mg DNB/kg diet)	Animal Number	9	10	11	12	13
30	1	187.0	189.7	189.0	194.9	190.3
	2	185.5	186.9	189.7	195.0	188.4
	3	188.1	189.8	191.6	196.1	189.8
	4	166.3	169.7	168.4	171.2	168.4
	5	163.4	165.4	169.0	172.7	169.8
	6	174.1	174.7	172.8	185.0	180.6
	7	178.9	181.5	183.1	186.0	184.5
	8	185.2	188.9	191.4	193.5	192.7
	9	182.1	186.3	185.7	200.1	195.5
	10	163.9	162.0	166.8	170.3	166.4
6	11	186.5	191.4	193.4	201.6	194.4
	12	187.5	190.4	190.9	196.6	192.3
	13	180.2	188.9	188.1	197.0	189.9
	14	179.0	181.2	185.5	191.1	188.6
	15	162.0	164.4	165.7	170.7	169.6
	16	168.3	171.6	178.0	176.7	174.8
	17	181.8	185.8	188.6	194.2	190.5
	18	175.5	178.6	178.1	188.8	183.2
	19	170.7	170.2	174.8	178.3	172.7
	20	173.5	173.2	175.2	180.0	177.4
1	21	191.8	194.2	193.6	199.1	197.4
	22	185.9	184.0	187.4	191.1	190.2
	23	192.4	201.5	203.0	203.3	200.7
	24	186.4	190.8	192.8	201.7	199.8
	25	183.4	187.5	188.1	191.9	191.6
	26	185.4	184.7	187.6	191.0	188.7
	27	170.2	171.2	176.0	175.3	177.7
	28	176.3	182.4	180.1	189.1	183.0
	29	168.2	170.6	172.2	177.6	173.2
	30	162.3	165.3	167.3	171.4	168.5
0	31	182.8	181.5	187.1	193.8	189.6
	32	173.1	170.1	173.5	178.4	172.1
	33	178.9	177.9	183.9	191.4	187.5
	34	165.7	168.6	168.1	175.5	172.2
	35	173.4	172.2	174.6	183.1	181.1
	36	178.6	178.0	180.7	186.8	181.8
	37	183.6	184.8	186.9	197.3	194.3
	38	178.0	178.4	180.0	186.8	182.6
	39	178.3	178.6	183.9	190.3	187.0
	40	167.6	167.9	169.4	173.5	170.6

# Weekly Body Weights (grams)/Males

Dose (mg DNB/kg diet)	Animal Number	Weeks							
		1	2	3	4	5	6	7	8
30	41	199.7	218.6	244.1	258.1	275.0	289.3	303.5	308.4
	42	189.0	202.2	220.8	234.2	246.3	254.0	268.8	271.9
	43	194.6	221.2	247.6	259.5	276.7	293.8	305.0	309.6
	44	203.2	222.8	245.0	263.9	274.6	289.7	311.3	315.6
	45	183.8	209.9	233.6	245.4	255.6	261.2	276.4	286.4
	46	192.5	210.9	233.7	245.7	260.5	274.8	285.3	291.6
	47	183.8	202.6	222.4	235.9	247.3	252.4	259.5	273.4
	48	189.2	218.2	236.6	252.4	266.2	281.3	300.2	300.0
	49	197.0	223.0	249.7	262.5	278.4	292.6	313.8	317.9
	50	173.5	188.6	207.7	215.4	224.9	242.9	251.6	257.4
6	51	213.8	236.4	263.6	279.4	301.1	317.5	338.3	350.2
	52	199.2	221.8	244.8	263.2	276.1	300.6	314.1	319.4
	53	183.7	205.5	229.2	235.9	251.3	267.0	277.4	279.1
	54	193.1	218.2	241.4	257.0	275.5	290.0	308.1	312.5
	55	193.4	210.7	235.7	252.4	266.8	285.6	299.2	302.0
	56	187.8	208.5	236.8	257.6	274.4	289.1	304.2	315.6
	57	200.0	222.3	242.2	256.8	271.2	288.7	305.8	306.0
	58	197.6	219.9	244.7	267.6	283.4	303.7	316.7	321.7
	59	190.6	212.6	240.3	259.7	277.1	295.3	314.6	320.3
	60	189.6	212.3	237.1	254.5	272.8	288.3	300.7	303.8
1	61	200.8	217.2	241.1	261.3	275.8	292.4	309.0	309.3
	62	199.1	219.1	238.7	253.7	271.9	285.5	304.0	303.3
	63	194.5	215.7	235.3	251.4	263.4	283.7	297.5	300.3
	64	192.7	217.3	235.3	252.8	265.4	276.5	280.4	288.3
	65	186.4	202.5	224.8	239.2	248.4	256.3	266.9	273.9
	66	187.6	211.2	243.5	261.7	276.2	295.2	309.8	312.2
	67	191.0	213.2	241.4	255.1	272.1	282.7	297.1	291.6
	68	188.1	210.7	240.3	258.4	273.6	288.5	304.1	310.1
	69	184.4	207.4	230.5	248.3	270.8	278.0	295.5	300.7
	70	188.9	204.8	233.2	243.0	259.4	278.3	291.6	294.0
0	71	202.6	217.4	235.2	256.2	266.4	278.1	291.8	295.6
	72	187.2	225.9	244.6	261.4	280.1	296.4	313.7	315.6
	73	190.8	209.9	232.4	249.1	260.9	272.1	282.3	285.4
	74	193.8	217.6	240.0	254.1	271.1	287.0	297.2	299.1
	75	193.0	218.3	239.2	256.0	270.1	284.0	303.2	310.5
	76	203.1	225.3	252.5	269.7	283.8	304.6	322.5	324.0
	77	198.5	224.9	249.8	269.8	289.5	308.4	320.1	328.3
	78	192.3	212.4	233.8	253.4	264.2	286.4	298.5	299.9
	79	178.8	202.6	228.1	250.1	263.4	276.6	287.8	294.1
	80	188.9	209.1	232.5	245.1	260.0	278.1	294.2	297.6

# Weekly Body Weights (grams)/Males

Dose (mg DNB/kg diet)	Animal Number	9	10	11	12	13
30	41	310.0	316.5	319.4	330.8	332.0
	42	273.1	279.1	282.7	293.5	289.4
	43	321.0	324.8	333.7	346.0	343.8
	44	320.0	328.7	337.6	347.7	346.5
	45	283.2	288.1	286.5	301.6	296.5
	46	293.2	295.6	300.3	309.8	312.1
	47	277.6	284.3	290.7	299.3	300.9
	48	300.4	307.0	312.3	317.1	317.6
	49	321.7	325.1	335.3	344.6	345.7
	50	260.0	260.2	262.9	274.7	271.3
6	51	348.7	357.1	363.6	377.0	378.0
	52	326.3	335.9	348.5	360.3	359.9
	53	282.8	285.8	289.0	296.6	296.3
	54	318.7	326.4	333.8	343.0	343.6
	55	304.8	303.2	309.4	315.2	312.8
	56	324.1	334.2	338.4	344.9	346.6
	57	302.5	311.9	319.5	327.5	329.6
	58	324.0	331.0	332.6	336.5	326.3
	59	323.3	330.6	340.9	351.8	350.8
	60	306.7	313.7	323.5	330.3	327.3
1	61	315.2	324.1	334.2	339.7	342.8
	62	312.0	315.8	323.6	336.6	339.6
	63	308.8	315.2	329.0	342.3	338.6
	64	288.0	302.4	307.2	312.6	317.1
	65	276.1	288.6	295.0	308.2	313.1
	66	314.1	326.3	333.6	344.0	339.9
	67	291.3	301.2	306.2	316.1	309.8
	68	314.1	321.0	336.3	338.8	340.0
	69	302.4	306.6	312.6	319.3	315.8
	70	295.9	301.8	296.9	308.9	304.9
0	71	295.2	300.3	301.1	308.4	309.8
	72	319.9	324.2	337.4	352.7	349.8
	73	283.5	291.5	292.1	292.4	290.4
	74	296.3	301.3	308.3	321.5	319.8
	75	307.7	317.8	319.3	342.2	338.1
	76	334.1	346.7	357.6	364.4	366.7
	77	339.9	343.4	349.1	364.3	358.0
	78	302.7	307.7	312.7	316.1	314.9
	79	290.2	298.9	292.7	295.3	292.2
	80	298.7	301.0	308.6	318.3	309.3

APPENDIX C

ORGAN WEIGHTS



GP-ANI NUMBER		BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER
1	1	183.29	1.317	1.027	4.928	0.719	0.560	2.689
1	2	185.59	1.389	0.937	5.132	0.748	0.505	2.765
1	3	182.61	1.203	0.883	4.926	0.659	0.484	2.698
1	4	166.16	1.254	1.065	4.588	0.755	0.641	2.761
1	5	161.76	1.106	0.805	4.099	0.684	0.498	2.534
1	6	172.44	1.214	0.845	4.565	0.704	0.490	2.647
1	7	178.98	1.198	1.057	4.340	0.669	0.591	2.425
1	8	185.83	1.281	0.943	4.567	0.689	0.507	2.458
1	9	186.79	1.206	0.918	5.032	0.646	0.491	2.694
1	10	159.86	1.126	0.842	4.456	0.704	0.527	2.787
2	11	186.22	1.340	1.085	4.820	0.720	0.583	2.588
2	12	181.42	1.161	0.983	4.945	0.640	0.542	2.726
2	13	180.32	1.164	0.868	4.444	0.646	0.481	2.465
2	14	182.73	1.195	0.972	4.629	0.654	0.532	2.533
2	15	163.68	1.089	0.848	4.215	0.665	0.518	2.575
2	16	167.23	1.128	0.900	4.277	0.675	0.538	2.558
2	17	179.38	1.165	1.051	4.767	0.649	0.586	2.657
2	18	171.97	1.205	0.855	4.804	0.701	0.497	2.794
2	19	163.37	1.122	1.025	4.301	0.687	0.627	2.633
2	20	168.33	1.187	1.061	4.630	0.705	0.630	2.751
3	21	187.17	1.245	0.984	4.904	0.665	0.526	2.620
3	22	180.68	1.227	0.931	4.346	0.679	0.515	2.405
3	23	190.36	1.231	0.997	4.736	0.647	0.524	2.488
3	24	191.90	1.285	0.969	4.804	0.670	0.505	2.503
3	25	183.40	1.179	0.814	4.507	0.643	0.444	2.457
3	26	179.02	1.196	0.964	4.925	0.668	0.538	2.751
3	27	168.04	1.140	0.990	4.397	0.678	0.589	2.617
3	28	174.28	1.174	0.949	5.083	0.674	0.545	2.917
3	29	165.00	1.045	0.789	3.892	0.633	0.478	2.359
3	30	159.92	1.100	0.863	4.061	0.688	0.540	2.539
4	31	178.56	1.177	0.903	4.615	0.659	0.506	2.585
4	32	166.47	1.134	0.917	4.651	0.681	0.551	2.794
4	33	178.65	1.169	1.014	4.576	0.654	0.568	2.561
4	34	163.44	1.087	1.004	4.297	0.665	0.614	2.629
4	35	169.47	1.136	0.937	4.701	0.670	0.553	2.774
4	36	173.50	1.236	0.950	4.601	0.712	0.548	2.652
4	37	180.23	1.239	1.179	4.996	0.687	0.654	2.772
4	38	174.38	1.191	0.970	4.402	0.683	0.556	2.524
4	39	179.29	1.240	0.996	4.617	0.692	0.556	2.575
4	40	160.85	1.106	0.853	3.850	0.688	0.530	2.394

GP-ANI NUMBER		BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN
1	1	183.29	0.668	1.728	0.586	0.364	0.943	0.320
1	2	185.59	0.735	1.785	0.571	0.396	0.962	0.308
1	3	182.61	0.632	1.851	0.511	0.346	1.014	0.280
1	4	166.16	0.634	1.797	0.510	0.382	1.081	0.307
1	5	161.76	0.660	1.756	0.500	0.408	1.086	0.309
1	6	172.44	0.611	1.772	0.420	0.354	1.028	0.244
1	7	178.98	0.664	1.728	0.515	0.371	0.965	0.288
1	8	185.83	0.723	1.875	0.567	0.389	1.009	0.305
1	9	186.79	0.751	1.626	0.545	0.402	0.870	0.292
1	10	159.86	0.765	1.698	0.492	0.479	1.062	0.308
2	11	186.22	0.734	1.848	0.421	0.394	0.992	0.226
2	12	181.42	0.618	1.785	0.437	0.341	0.984	0.241
2	13	180.32	0.705	1.793	0.440	0.391	0.994	0.244
2	14	182.73	0.597	1.817	0.413	0.327	0.994	0.226
2	15	163.68	0.585	1.739	0.392	0.357	1.062	0.239
2	16	167.23	0.611	1.751	0.454	0.365	1.047	0.271
2	17	179.38	0.629	1.745	0.457	0.351	0.973	0.255
2	18	171.97	0.719	1.743	0.435	0.418	1.014	0.253
2	19	163.37	0.603	1.805	0.407	0.369	1.105	0.249
2	20	168.33	0.600	1.771	0.431	0.356	1.052	0.256
3	21	187.17	0.766	1.820	0.426	0.409	0.972	0.228
3	22	180.68	0.575	1.692	0.419	0.318	0.936	0.232
3	23	190.36	0.670	1.754	0.461	0.352	0.921	0.242
3	24	191.90	0.716	1.807	0.432	0.373	0.942	0.225
3	25	183.40	0.669	1.834	0.439	0.365	1.000	0.239
3	26	179.02	0.648	1.765	0.410	0.362	0.986	0.229
3	27	168.04	0.613	1.708	0.393	0.365	1.016	0.234
3	28	174.28	0.744	1.693	0.454	0.427	0.971	0.261
3	29	165.00	0.646	1.736	0.384	0.392	1.052	0.233
3	30	159.92	0.587	1.732	0.421	0.367	1.083	0.263
4	31	178.56	0.633	1.781	0.427	0.355	0.997	0.239
4	32	166.47	0.638	1.707	0.513	0.383	1.025	0.308
4	33	178.65	0.615	1.701	0.437	0.344	0.952	0.245
4	34	163.44	0.656	1.711	0.408	0.401	1.047	0.250
4	35	169.47	0.602	1.734	0.482	0.355	1.023	0.284
4	36	173.50	0.578	1.784	0.419	0.333	1.028	0.241
4	37	180.23	0.748	1.785	0.465	0.415	0.990	0.258
4	38	174.38	0.642	1.751	0.482	0.368	1.004	0.276
4	39	179.29	0.644	1.752	0.438	0.359	0.977	0.244
4	40	160.85	0.624	1.685	0.384	0.388	1.048	0.239

GP-ANI NUMBER		BODY WEIGHT	ADRENAL WEIGHT	THYMUS WEIGHT	OVARIES WEIGHT	% ADRENAL	% THYMUS	% OVARIES
1	1	183.29	0.070	0.203	0.121	0.038	0.111	0.066
1	2	185.59	0.053	0.236	0.153	0.029	0.127	0.082
1	3	182.61	0.059	0.143	0.119	0.032	0.078	0.065
1	4	166.16	0.074	0.211	0.143	0.045	0.127	0.086
1	5	161.76	0.045	0.189	0.127	0.028	0.117	0.079
1	6	172.44	0.059	0.148	0.102	0.034	0.086	0.059
1	7	178.98	0.072	0.238	0.121	0.040	0.133	0.068
1	8	185.83	0.056	0.237	0.120	0.030	0.128	0.065
1	9	186.79	0.056	0.200	0.093	0.030	0.107	0.050
1	10	159.86	0.054	0.184	0.099	0.034	0.115	0.062
2	11	186.22	0.091	0.248	0.213	0.049	0.133	0.114
2	12	181.42	0.046	0.237	0.125	0.025	0.131	0.069
2	13	180.32	0.053	0.214	0.129	0.029	0.119	0.072
2	14	182.73	0.069	0.242	0.139	0.038	0.132	0.076
2	15	163.68	0.060	0.254	0.132	0.037	0.155	0.081
2	16	167.23	0.066	0.189	0.129	0.039	0.113	0.077
2	17	179.38	0.060	0.214	0.135	0.033	0.119	0.075
2	18	171.97	0.058	0.169	0.117	0.034	0.098	0.068
2	19	163.37	0.053	0.171	0.164	0.032	0.105	0.100
2	20	168.33	0.065	0.206	0.139	0.039	0.122	0.083
3	21	187.17	0.057	0.212	0.121	0.030	0.113	0.065
3	22	180.68	0.043	0.238	0.097	0.024	0.132	0.054
3	23	190.36	0.063	0.219	0.141	0.033	0.115	0.074
3	24	191.90	0.058	0.234	0.144	0.030	0.122	0.075
3	25	183.40	0.048	0.221	0.145	0.026	0.121	0.079
3	26	179.02	0.066	0.284	0.207	0.037	0.159	0.116
3	27	168.04	0.057	0.134	0.113	0.034	0.080	0.067
3	28	174.28	0.077	0.170	0.185	0.044	0.098	0.106
3	29	165.00	0.046	0.195	0.177	0.028	0.118	0.107
3	30	159.92	0.062	0.176	0.145	0.039	0.110	0.091
4	31	178.56	0.052	0.205	0.139	0.029	0.115	0.078
4	32	166.47	0.055	0.160	0.097	0.033	0.096	0.058
4	33	178.65	0.071	0.243	0.151	0.040	0.136	0.085
4	34	163.44	0.071	0.201	0.175	0.043	0.123	0.107
4	35	169.47	0.065	0.225	0.143	0.038	0.133	0.084
4	36	173.50	0.079	0.218	0.143	0.046	0.126	0.082
4	37	180.23	0.078	0.180	0.169	0.043	0.100	0.094
4	38	174.38	0.074	0.203	0.195	0.042	0.116	0.112
4	39	179.29	0.060	0.224	0.138	0.033	0.125	0.077
4	40	160.85	0.060	0.188	0.090	0.037	0.117	0.056

GP-ANI NUMBER	BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER
5 41	318.39	1.981	1.172	8.701	0.622	0.368	2.733
5 42	279.33	1.758	1.278	7.444	0.629	0.458	2.665
5 43	330.64	2.207	1.205	9.737	0.667	0.364	2.945
5 44	331.32	2.334	1.486	10.593	0.704	0.449	3.197
5 45	287.23	2.006	1.355	8.264	0.698	0.472	2.877
5 46	300.04	2.003	1.180	8.426	0.668	0.393	2.808
5 47	283.85	1.879	1.307	7.405	0.662	0.460	2.609
5 48	303.91	1.987	1.362	8.090	0.654	0.448	2.662
5 49	334.07	2.255	1.281	8.996	0.675	0.383	2.693
5 50	258.54	1.936	1.247	6.686	0.749	0.482	2.586
6 51	361.56	2.589	1.629	10.062	0.716	0.451	2.783
6 52	343.98	2.440	1.474	9.853	0.709	0.429	2.864
6 53	282.38	1.996	1.379	7.584	0.707	0.488	2.686
6 54	324.38	2.123	1.685	9.461	0.654	0.519	2.917
6 55	298.05	1.967	1.278	7.793	0.660	0.429	2.615
6 56	331.27	2.247	1.548	9.353	0.678	0.467	2.823
6 57	316.51	2.330	1.391	9.349	0.736	0.439	2.954
6 58	310.74	2.129	1.486	8.413	0.685	0.478	2.707
6 59	338.27	2.433	1.344	9.336	0.719	0.397	2.760
6 60	316.25	2.284	1.567	8.806	0.722	0.495	2.785
7 61	323.82	2.307	1.326	9.253	0.712	0.409	2.857
7 62	327.53	2.312	1.478	9.733	0.706	0.451	2.972
7 63	326.18	2.227	1.254	9.542	0.683	0.384	2.925
7 64	304.19	2.065	1.193	8.170	0.679	0.392	2.686
7 65	298.95	2.074	1.346	7.960	0.694	0.450	2.663
7 66	330.53	2.183	1.437	9.854	0.660	0.435	2.981
7 67	298.94	2.105	1.392	8.322	0.704	0.466	2.784
7 68	330.36	2.354	1.216	9.228	0.713	0.368	2.793
7 69	301.75	1.879	1.218	7.794	0.623	0.404	2.583
7 70	299.93	2.077	1.131	8.551	0.692	0.377	2.851
8 71	292.06	2.043	1.292	8.326	0.700	0.442	2.851
8 72	332.50	2.360	1.625	10.418	0.710	0.489	3.133
8 73	279.62	1.854	1.265	7.366	0.663	0.452	2.634
8 74	308.12	2.119	1.560	8.639	0.688	0.506	2.804
8 75	315.04	2.196	1.445	9.436	0.697	0.459	2.995
8 76	353.19	2.375	1.585	10.262	0.672	0.449	2.906
8 77	345.70	2.250	1.422	9.467	0.651	0.411	2.739
8 78	300.20	2.000	1.173	8.225	0.666	0.391	2.740
8 79	285.36	1.853	1.159	7.403	0.649	0.406	2.594
8 80	294.04	1.957	1.147	7.890	0.666	0.390	2.683

GP-ANI NUMBER		BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN
5	41	318.39	1.004	1.970	0.711	0.315	0.619	0.223
5	42	279.33	0.843	1.740	0.688	0.302	0.623	0.246
5	43	330.64	1.048	2.004	0.794	0.317	0.606	0.240
5	44	331.32	0.938	1.844	0.768	0.283	0.557	0.232
5	45	287.23	0.885	1.864	0.672	0.308	0.649	0.234
5	46	300.04	0.911	1.850	0.702	0.304	0.617	0.234
5	47	283.85	0.807	1.811	0.759	0.284	0.638	0.267
5	48	303.91	0.881	1.911	0.709	0.290	0.629	0.233
5	49	334.07	1.038	1.892	0.808	0.311	0.566	0.242
5	50	258.54	0.809	1.801	0.692	0.313	0.697	0.268
6	51	361.56	1.247	1.943	0.721	0.345	0.537	0.199
6	52	343.98	1.057	1.890	0.686	0.307	0.549	0.199
6	53	282.38	0.912	1.811	0.568	0.323	0.641	0.201
6	54	324.38	1.101	1.988	0.627	0.339	0.613	0.193
6	55	298.05	0.997	1.933	0.582	0.335	0.649	0.195
6	56	331.27	0.961	1.867	0.681	0.290	0.564	0.206
6	57	316.51	1.104	1.746	0.624	0.349	0.552	0.197
6	58	310.74	1.071	1.909	0.686	0.345	0.614	0.221
6	59	338.27	1.021	1.798	0.782	0.302	0.532	0.231
6	60	316.25	1.051	1.845	0.679	0.332	0.583	0.215
7	61	323.82	0.970	1.875	0.578	0.300	0.579	0.178
7	62	327.53	1.064	1.943	0.603	0.325	0.593	0.184
7	63	326.18	1.042	1.928	0.630	0.319	0.591	0.193
7	64	304.19	0.945	1.991	0.609	0.311	0.655	0.200
7	65	298.95	0.917	1.884	0.619	0.307	0.630	0.207
7	66	330.53	0.920	1.943	0.653	0.278	0.588	0.198
7	67	298.94	0.972	1.850	0.554	0.325	0.619	0.185
7	68	330.36	1.050	1.916	0.632	0.318	0.580	0.191
7	69	301.75	1.002	1.927	0.568	0.332	0.639	0.188
7	70	299.93	0.956	1.920	0.587	0.319	0.640	0.196
8	71	292.06	0.953	1.916	0.557	0.326	0.656	0.191
8	72	332.50	0.923	1.940	0.690	0.278	0.583	0.208
8	73	279.62	0.820	1.920	0.587	0.293	0.687	0.210
8	74	308.12	0.824	1.878	0.637	0.267	0.610	0.207
8	75	315.04	1.016	1.944	0.743	0.322	0.617	0.236
8	76	353.19	1.139	1.954	0.669	0.322	0.553	0.189
8	77	345.70	1.090	1.981	0.667	0.315	0.573	0.193
8	78	300.20	0.893	1.924	0.567	0.297	0.641	0.189
8	79	285.36	0.982	1.924	0.542	0.344	0.674	0.190
8	80	294.04	0.980	1.816	0.535	0.333	0.618	0.182

GP-ANI NUMBER	BODY WEIGHT	ADRENAL WEIGHT	THYMUS WEIGHT	TESTES WEIGHT	% ADRENAL	% THYMUS	% TESTES
5 41	318.39	0.062	0.251	1.361	0.019	0.079	0.427
5 42	279.33	0.046	0.290	2.756	0.016	0.104	0.987
5 43	330.64	0.057	0.256	2.804	0.017	0.077	0.848
5 44	331.32	0.050	0.239	3.542	0.015	0.072	1.069
5 45	287.23	0.054	0.231	2.970	0.019	0.080	1.034
5 46	300.04	0.047	0.189	2.484	0.016	0.063	0.828
5 47	283.85	0.053	0.240	3.395	0.019	0.085	1.196
5 48	303.91	0.052	0.377	3.000	0.017	0.124	0.987
5 49	334.07	0.047	0.280	2.700	0.014	0.084	0.808
5 50	258.54	0.058	0.227	4.020	0.022	0.088	1.555
6 51	361.56	0.077	0.325	7.085	0.021	0.090	1.960
6 52	343.98	0.073	0.259	6.695	0.021	0.075	1.946
6 53	282.38	0.065	0.256	5.347	0.023	0.091	1.894
6 54	324.38	0.092	0.313	6.550	0.028	0.096	2.019
6 55	298.05	0.060	0.263	4.233	0.020	0.088	1.420
6 56	331.27	0.048	0.437	4.703	0.014	0.132	1.420
6 57	316.51	0.078	0.112	6.188	0.025	0.035	1.955
6 58	310.74	0.081	0.276	6.371	0.026	0.089	2.050
6 59	338.27	0.038	0.285	4.508	0.011	0.084	1.333
6 60	316.25	0.063	0.263	6.709	0.020	0.083	2.121
7 61	323.82	0.040	0.244	4.592	0.012	0.075	1.418
7 62	327.53	0.091	0.324	6.508	0.028	0.099	1.987
7 63	326.18	0.037	0.250	4.682	0.011	0.077	1.435
7 64	304.19	0.042	0.199	4.518	0.014	0.065	1.485
7 65	298.95	0.040	0.232	4.410	0.013	0.078	1.475
7 66	330.53	0.043	0.455	4.712	0.013	0.138	1.426
7 67	298.94	0.067	0.275	6.210	0.022	0.092	2.077
7 68	330.36	0.055	0.272	4.040	0.017	0.082	1.223
7 69	301.75	0.046	0.380	4.399	0.015	0.126	1.458
7 70	299.93	0.056	0.277	4.148	0.019	0.092	1.383
8 71	292.06	0.055	0.221	4.462	0.019	0.076	1.528
8 72	332.50	0.049	0.306	4.757	0.015	0.092	1.431
8 73	279.62	0.052	0.284	4.431	0.019	0.102	1.585
8 74	308.12	0.048	0.194	4.839	0.016	0.063	1.570
8 75	315.04	0.052	0.239	4.574	0.017	0.076	1.452
8 76	353.19	0.096	0.240	7.556	0.027	0.068	2.139
8 77	345.70	0.065	0.312	4.853	0.019	0.090	1.404
8 78	300.20	0.043	0.217	4.388	0.014	0.072	1.462
8 79	285.36	0.060	0.231	3.460	0.021	0.081	1.213
8 80	294.04	0.056	0.259	3.996	0.019	0.088	1.359

APPENDIX D  
HEMATOLOGY DATA

# Hematology Data/Females 45 Day

DOSE GROUPS	ANIMALS	METHB	WBC COUNT	RBC COUNT	HGB	HCT	MCV
(mg DNB/kg) diet	#	%	thsn/ cu mm	mill/ cu mm	g/dl	%	cumicr
30	1-361	3.9	3.7	7.45	14.1	40.9	54.9
	1-362	3.9	3.2	7.38	14.0	40.2	54.5
	1-363	4.9	4.7	7.35	13.8	39.4	53.7
	1-364	4.3	3.7	7.25	13.8	40.2	55.5
	1-365	3.3	4.2	7.48	14.1	40.7	54.4
6	2-366	1.4	4.3	8.07	15.0	42.4	52.5
	2-367	1.4	3.1	7.89	14.8	41.0	52.0
	2-368	1.5	3.5	7.91	14.6	41.2	52.2
	2-369	1.6	3.6	8.10	15.3	43.2	53.3
	2-370	1.6	2.8	8.32	15.6	43.9	52.7
1	3-371	0.7	3.7	7.99	15.0	41.9	52.5
	3-372	0.8	2.7	8.13	15.1	43.9	54.0
	3-373	0.2	2.4	7.69	14.3	40.2	52.3
	3-374	0.7	3.0	7.83	14.6	40.7	52.0
	3-375	1.1	3.4	7.94	14.9	41.7	52.5
0	4-376	0.2	3.5	8.22	15.2	42.5	51.7
	4-377	0.4	3.2	7.93	14.9	42.0	52.9
	4-378	0.8	2.4	7.86	14.6	41.0	52.2
	4-379	1.3	3.5	8.19	15.2	43.0	52.5
	4-380	0.6	3.1	8.31	15.4	43.6	52.5



# Hematology Data/Females 45 Day

DOSE GROUPS	ANIMALS	MCH	MCHC	PLAT	NEUTRO- PHILS	LYMPHO- CYTES	RETIC	HEINZ BODIES
(mg DNB/kg)				thsn/ cu mm				
diet	#	picogm	g/dl		%	%	%	%
30	1-361	18.9	34.5	812	13.7	81.8	5.1	0.0
	1-362	19.0	34.9	881	22.8	71.7	4.8	0.0
	1-363	18.8	35.1	818	11.8	85.5	4.0	0.0
	1-364	19.0	34.2	809	16.6	79.7	4.5	0.0
	1-365	18.9	34.7	750	13.5	84.1	4.6	0.0
6	2-366	18.6	35.3	797	21.0	76.5	2.4	0.0
	2-367	18.7	36.0	767	12.5	84.1	2.7	0.0
	2-368	18.5	35.5	776	18.0	78.8	2.5	0.0
	2-369	18.9	35.5	780	23.5	74.4	2.5	0.0
	2-370	18.7	35.5	769	18.7	77.6	2.7	0.0
1	3-371	18.8	35.8	808	17.1	79.0	2.2	0.0
	3-372	18.6	34.4	757	26.6	69.7	2.3	0.0
	3-373	18.6	35.5	783	14.0	82.6	2.2	0.0
	3-374	18.6	35.8	741	14.6	81.4	2.1	0.0
	3-375	18.8	35.7	810	22.5	73.9	2.9	0.0
0	4-376	18.5	35.7	722	18.3	77.4	1.8	0.0
	4-377	18.7	35.4	748	19.8	77.1	2.1	0.0
	4-378	18.6	35.6	738	16.9	79.5	2.0	0.0
	4-379	18.6	35.4	835	17.2	78.9	3.0	0.0
	4-380	18.5	35.3	752	20.2	76.6	1.8	0.0

# Hematology Data/Females

90 Day

DOSE GROUPS	ANIMALS	METHB	WBC COUNT	RBC COUNT	HGB	HCT	MCV
(mg DNB/kg)			thsn/	mill/			
diet	#	%	cu mm	cu mm	g/dl	%	cumicr
30	1-01	4.0	4.1	7.26	14.2	39.8	54.8
	1-02	4.1	3.6	7.07	13.9	38.3	54.2
	1-03	3.5	3.8	7.19	14.0	38.4	53.3
	1-04	3.9	3.8	7.34	*	39.1	53.3
	1-05	3.8	2.6	7.24	14.1	39.3	54.3
	1-06	3.4	3.7	7.41	14.2	39.3	53.0
	1-07	3.9	4.3	7.32	*	38.8	53.1
	1-08	3.6	2.9	7.29	14.2	39.3	53.9
	1-09	3.6	4.7	7.77	14.9	43.2	55.6
	1-10	3.9	3.7	7.41	14.2	40.6	54.8
6	2-11	1.6	2.9	7.76	15.1	40.8	52.6
	2-12	1.6	3.0	7.77	15.0	40.7	52.4
	2-13	1.8	4.4	7.89	15.4	41.8	52.9
	2-14	1.8	3.3	8.01	15.4	41.7	52
	2-15	1.9	3.8	8.04	15.5	42.3	52.6
	2-16	1.4	3.0	7.77	15.0	40.6	52.3
	2-17	1.8	2.8	7.54	14.8	39.3	52.1
	2-18	1.6	2.0	7.97	15.2	41.5	52.1
	2-19	1.0	3.1	7.47	14.6	38.8	51.9
	2-20	1.4	2.0	7.92	15.3	41.3	52.2
1	3-21	1.7	2.7	7.94	15.5	41.8	52.6
	3-22	0.9	1.6	7.74	15.3	39.6	51.2
	3-23	0.6	2.5	8.19	15.5	42.8	52.3
	3-24	1.0	3.4	7.91	15.6	41.2	52.1
	3-25	1.1	3.3	7.94	15.4	41.3	51.9
	3-26	0.5	3.6	8.16	15.6	43.2	52.9
	3-27	1.4	3.5	8.00	15.5	41.6	52.1
	3-28	1.0	2.8	8.04	15.2	42.7	53.1
	3-29	2.1	4.1	8.26	*	43.2	52.2
	3-30	0.8	2.8	8.06	15.4	42.2	52.3
0	4-31	0.3	3.3	8.02	15.3	42.0	52.4
	4-32	0.5	3.6	7.65	14.7	40.3	52.6
	4-33	0.6	3.8	7.91	15.4	40.8	51.5
	4-34	0.1	2.2	7.70	15.2	41.6	54.0
	4-35	1.0	3.7	7.95	15.5	41.9	52.6
	4-36	0.5	3.6	7.76	14.9	40.7	52.5
	4-37	1.2	3.1	8.02	15.6	41.4	51.6
	4-38	0.7	2.8	7.88	15.2	41.1	52.2
	4-39	0.9	4.0	8.13	15.7	42.2	51.9
	4-40	1.4	4.6	8.12	15.8	42.5	52.3

\* Data unavailable

## Hematology Data/Females

90 Day

DOSE GROUPS	ANIMALS	MCH	MCHC	PLAT	NEUTRO- PHILS	LYMPHO- CYTES	RETIC	HEINZ BODIES
(mg DNB/kg)								
diet	#	picogm	g/dl	thsn/ cu mm	%	%	%	%
30	1-01	19.6	35.8	729	18.3	77.9	3.7	0.0
	1-02	19.7	36.3	703	21.2	75.8	3.5	0.0
	1-03	19.4	36.4	704	21.4	75.7	2.9	0.0
	1-04	*	*	723	5.9	74.0	2.8	0.0
	1-05	19.4	35.8	709	17.0	79.9	4.7	0.0
	1-06	19.2	36.2	631	18.1	79.4	3.7	0.0
	1-07	*	*	703	8.8	66.8	4.2	0.0
	1-08	19.5	36.3	694	28.8	66.1	3.6	0.0
	1-09	19.2	34.6	688	20.2	77.1	3.3	0.0
	1-10	19.2	34.9	690	13.2	83.8	3.2	0.0
6	2-11	19.5	37.1	660	17.1	79.0	1.9	0.0
	2-12	19.3	36.8	617	17.7	77.9	1.7	0.0
	2-13	19.5	36.9	717	15.2	82.1	2.1	0.0
	2-14	19.2	36.9	682	20.5	76.9	1.9	0.0
	2-15	19.3	36.6	597	16.8	79.7	2.1	0.0
	2-16	19.3	36.9	632	15.6	81.6	1.8	0.0
	2-17	19.6	37.6	639	19.2	76.6	1.7	0.0
	2-18	19.1	36.6	642	31.5	62.8	2.0	0.0
	2-19	19.5	37.5	709	26.6	69.0	2.1	0.0
	2-20	19.4	37.1	586	18.5	78.1	1.9	0.0
1	3-21	19.6	37.2	649	21.6	73.9	1.9	0.0
	3-22	19.8	38.7	622	20.7	75.6	1.8	0.0
	3-23	19.0	36.2	574	31.4	56.7	1.5	0.0
	3-24	19.7	37.8	641	17.5	78.8	1.7	0.0
	3-25	19.4	37.3	652	23.6	72.1	2.0	0.0
	3-26	19.1	36.1	659	18.2	78.0	1.6	0.0
	3-27	19.4	37.2	678	28.2	68.0	2.1	0.0
	3-28	18.9	35.7	599	21.0	75.4	1.8	0.0
	3-29	*	*	548	9.1	68.2	2.0	0.0
	3-30	19.1	36.6	642	14.9	81.7	1.9	0.0
0	4-31	19.1	36.4	664	23.6	73.3	1.5	0.0
	4-32	19.2	36.4	685	22.3	73.7	2.4	0.0
	4-33	19.4	37.8	685	22.4	74.0	1.7	0.0
	4-34	19.8	36.6	645	21.3	75.0	1.4	0.0
	4-35	19.4	36.9	577	14.9	82.7	1.6	0.0
	4-36	19.2	36.5	673	18.9	78.2	1.3	0.0
	4-37	19.4	37.6	603	24.2	71.6	2.0	0.0
	4-38	19.3	37.0	632	20.4	76.6	2.2	0.0
	4-39	19.3	37.2	667	12.8	85.0	1.7	0.0
	4-40	19.5	37.2	592	13.3	83.6	1.6	0.0

\*Data unavailable

# Hematology Data/Males 45 Day

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	METHB %	WBC COUNT thsn/ cu mm	RBC COUNT mill/ cu mm	HGB g/dl	HCT %	MCV cubicr
30	5-381	6.1	4.3	8.22	14.2	41.9	51.0
	5-382	4.3	5.0	8.39	14.5	43.6	52.0
	5-383	3.4	4.8	8.31	14.3	42.7	51.4
	5-384	4.1	5.5	8.23	14.3	42.1	51.2
	5-385	4.3	2.9	8.05	13.9	41.5	51.5
6	6-386	1.0	5.9	8.59	14.4	42.5	49.5
	6-387	1.1	4.1	8.95	15.2	44.7	50.0
	6-388	0.5	4.9	9.04	15.1	44.9	19.6
	6-389	2.2	3.7	9.19	15.6	45.4	49.4
	6-390	1.7	3.6	8.99	15.1	44.7	49.8
1	7-391	0.9	2.9	8.78	14.9	43.6	49.6
	7-392	0.4	5.0	9.03	15.3	45.0	49.9
	7-393	0.3	3.5	8.85	15.0	43.2	48.7
	7-394	1.3	4.4	8.91	15.5	44.9	50.4
	7-395	1.0	4.4	9.12	15.4	45.5	49.9
0	8-396	0.5	3.4	9.16	15.6	44.7	48.8
	8-397	0.9	3.4	8.88	15.0	43.6	49.1
	8-398	0.2	4.2	8.98	15.4	44.3	49.3
	8-399	0.7	5.6	8.96	15.2	44.4	49.6
	8-400	0.6	4.0	8.93	15.1	44.6	49.9

Hematology Data/Males  
45 Day

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	MCH picogm	MCHC g/dl	PLAT thsn/ cu mm	NEUTRO- PHILS %	LYMPHO- CYTES %	RETIC %	HEINZ BODIES %
30	5-381	17.2	33.8	727	18.6	78.2	4.0	0.0
	5-382	17.2	33.1	657	17.0	79.6	5.0	0.0
	5-383	17.3	33.6	804	22.0	74.5	4.4	0.0
	5-384	17.3	33.9	783	17.9	79.1	4.8	0.0
	5-385	17.3	33.5	536	17.8	79.8	4.3	0.0
6	6-386	16.8	33.9	792	27.4	69.1	3.3	0.0
	6-387	17.0	34.0	770	25.1	71.6	3.5	0.0
	6-388	16.7	33.6	775	21.0	75.6	3.2	0.0
	6-389	17.0	34.4	636	16.7	80.8	2.8	0.0
	6-390	16.8	33.6	782	25.6	70.7	3.2	0.0
1	7-391	17.0	34.2	824	23.2	73.5	3.3	0.0
	7-392	17.0	34.0	879	25.8	70.5	3.0	0.0
	7-393	16.9	34.7	747	21.4	75.6	2.5	0.0
	7-394	17.4	34.6	672	19.4	77.5	2.1	0.0
	7-395	16.9	33.9	766	21.8	75.4	3.2	0.0
0	8-396	17.0	34.8	757	22.2	74.2	2.5	0.0
	8-397	16.9	34.4	780	21.0	75.4	2.4	0.0
	8-398	17.1	34.8	736	26.1	70.5	2.8	0.0
	8-399	17.0	34.3	789	29.1	67.2	2.3	0.0
	8-400	16.9	33.9	745	20.1	76.5	2.5	0.0

Hematology Data/Males  
90 Day

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	METHB %	WBC COUNT thsn/ cu mm	RBC COUNT mill/ cu mm	HGB g/dl	HCT %	MCV cumicr
30	5-41	4.3	5.5	8.47	14.9	42.4	50.2
	5-42	3.7	4.5	8.17	14.7	42.5	52.0
	5-43	5.2	6.6	8.17	14.2	40.6	49.7
	5-44	4.1	3.8	8.27	14.4	41.3	50.0
	5-45	3.8	4.1	8.05	14.4	41.0	50.9
	5-46	4.0	3.5	8.26	14.6	42.1	50.9
	5-47	4.3	3.4	7.99	14.5	40.9	51.1
	5-48	3.8	4.9	8.00	14.2	40.9	51.1
	5-49	4.2	3.2	8.06	14.5	40.5	50.3
	5-50	3.7	3.1	7.97	14.4	40.3	50.6
6	6-51	2.0	4.6	9.07	15.3	43.1	47.5
	6-52	1.9	2.3	8.67	15.0	41.5	47.8
	6-53	0.8	2.4	9.26	15.8	45.7	49.4
	6-54	1.5	3.9	8.94	15.2	43.6	48.8
	6-55	1.2	3.0	8.55	14.8	40.8	47.7
	6-56	1.6	4.0	9.12	15.6	44.4	48.7
	6-57	1.3	4.3	8.98	15.4	43.0	47.9
	6-58	1.6	2.4	8.71	15.3	41.6	47.8
	6-59	1.9	3.4	8.79	15.0	42.9	48.8
	6-60	0.8	5.2	9.17	15.7	44.7	48.7
1	7-61	0.9	3.8	9.34	15.8	45.1	48.3
	7-62	0.9	4.6	9.31	15.9	44.8	48.2
	7-63	0.6	3.6	8.90	15.2	43.1	48.4
	7-64	0.9	3.7	8.88	15.6	44.0	49.5
	7-65	0.6	2.4	8.43	15.1	41.4	49.1
	7-66	1.6	3.2	9.06	15.6	44.3	48.9
	7-67	0.4	3.3	8.92	15.5	43.8	49.0
	7-68	0.7	3.3	9.22	15.9	44.7	48.5
	7-69	0.8	3.7	9.05	15.8	44.8	49.5
	7-70	0.4	3.3	8.90	15.2	43.4	48.7
0	8-71	0.7	3.2	9.20	16.1	45.6	49.6
	8-72	0.8	3.3	9.15	15.7	45.0	49.2
	8-73	0.6	6.2	8.80	15.6	43.6	49.6
	8-74	0.8	3.1	8.79	15.3	43.1	49.0
	8-75	0.6	4.7	8.81	15.3	43.9	49.8
	8-76	0.8	4.2	9.32	15.8	44.8	48.0
	8-77	0.6	3.9	9.09	15.8	44.9	49.4
	8-78	0.9	4.2	9.06	15.6	43.5	48.0
	8-79	0.7	4.7	8.76	15.4	43.4	49.5
	8-80	1.0	3.7	8.90	15.8	43.2	48.5

# Hematology Data/Males

## 90 Day

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	MCH picogm	MCHC g/dl	PLAT thsn/ cu mm	NEUTRO- PHILS %	LYMPHO- CYTES %	RETIC %	HEINZ BODIES %
30	5-41	17.6	35.1	704	22.5	74.5	2.7	0.0
	5-42	78.0	34.6	643	19.0	77.8	3.5	0.0
	5-43	17.4	35.0	666	16.2	81.3	3.4	0.0
	5-44	17.4	34.7	645	25.2	72.3	3.0	0.0
	5-45	17.9	35.2	563	23.1	74.0	3.2	0.0
	5-46	17.7	34.7	662	20.9	75.9	2.4	0.0
	5-47	18.1	35.4	711	16.9	80.5	3.0	0.0
	5-48	17.8	34.8	611	12.1	85.3	3.5	0.0
	5-49	17.9	35.7	693	21.8	74.2	4.1	0.0
	5-50	18.1	35.7	698	21.7	75.5	2.7	0.0
6	6-51	16.8	35.4	663	20.4	75.8	1.7	0.0
	6-52	17.3	36.1	678	24.1	72.0	1.8	0.0
	6-53	17.1	34.5	645	21.5	74.7	2.6	0.0
	6-54	17.0	34.8	602	20.1	77.0	1.8	0.0
	6-55	17.3	36.3	596	24.3	71.5	2.0	0.0
	6-56	17.1	35.2	635	15.4	80.5	2.0	0.0
	6-57	17.1	35.8	724	18.0	78.4	1.4	0.0
	6-58	17.6	36.8	*	27.2	69.0	1.5	0.0
	6-59	17.1	35.0	562	19.8	75.5	2.5	0.0
	6-60	17.1	35.1	613	14.5	78.9	2.2	0.0
1	7-61	16.9	35.1	583	27.2	68.4	1.6	0.0
	7-62	17.1	35.5	633	19.6	78.0	1.5	0.0
	7-63	17.0	35.2	655	17.9	78.7	1.9	0.0
	7-64	17.5	35.3	657	22.9	72.7	1.6	0.0
	7-65	17.9	36.5	638	25.4	71.8	1.7	0.0
	7-66	17.3	35.3	592	16.9	80.4	1.8	0.0
	7-67	17.3	35.3	613	23.2	72.1	1.7	0.0
	7-68	17.2	35.6	583	19.5	77.4	1.7	0.0
	7-69	17.4	35.2	*	19.4	76.9	2.0	0.0
	7-70	17.1	35.0	501	18.3	78.4	1.8	0.0
0	8-71	17.5	35.3	530	20.9	76.2	1.9	0.0
	8-72	17.2	34.9	641	20.6	76.4	1.6	0.0
	8-73	17.8	35.8	628	16.5	80.4	1.5	0.0
	8-74	17.4	35.5	691	26.6	69.9	1.8	0.0
	8-75	17.3	34.8	1014	24.8	70.5	1.9	0.0
	8-76	17.0	35.3	721	19.4	76.7	1.2	0.0
	8-77	17.3	35.1	671	19.5	76.2	2.2	0.0
	8-78	17.2	35.8	645	21.5	76.3	2.2	0.0
	8-79	17.6	35.6	*	17.6	78.8	1.7	0.0
	8-80	17.8	36.6	534	21.4	75.0	1.3	0.0

\*Data unavailable

APPENDIX E

CLINICAL CHEMISTRY  
DATA



## Clinical Chemistries/Females

45 Day

DOSE GROUPS	ANIMALS	GLUCOSE	BUN	CREAT	SODIUM	POTASSIUM	CHOL
(mg DNB/kg)							
diet	#	mg/dl	mg/dl	mg/dl	mmol/l	mmol/l	mg/dl
30	1-361	108	21	0.6	140	4.8	96
	1-362	102	19	0.5	140	4.3	98
	1-363	99	26	0.6	140	4.1	91
	1-364	101	21	0.6	139	4.5	95
	1-365	121	22	0.6	141	4.2	90
6	2-366	133	25	0.5	141	3.9	86
	2-367	107	21	0.5	140	4.4	96
	2-368	130	24	0.5	140	4.2	86
	2-369	113	22	0.6	141	4.6	94
	2-370	105	22	0.6	142	4.7	92
1	3-371	125	21	0.5	141	4.4	82
	3-372	166	26	0.5	140	5.8	82
	3-373	104	20	0.5	142	4.1	75
	3-374	119	23	0.5	140	4.6	80
	3-375	131	23	0.5	140	4.6	80
0	4-376	104	20	0.6	141	4.5	85
	4-377	92	17	0.5	141	4.1	94
	4-378	90	19	0.5	141	4.3	91
	4-379	107	24	0.6	141	4.5	82
	4-380	120	20	0.6	140	4.2	93

Clinical Chemistries/Females  
45 Day

DOSE GROUPS	ANIMALS	AST	ALT	PHOS	AP	Ca	TOTAL BILIRUBIN	TOTAL PROTEIN	ALB	TRIG
(mg DNB/kg)										
diet	#	U/L	U/L	mg/dl	U/L	mg/dl	mg/dl	g/dl	g/dl	mg/dl
30	1-361	181	74	9.7	106	10.1	0.2	5.9	4.5	37
	1-362	118	32	8.3	91	10.3	0.1	6.2	4.8	31
	1-363	118	39	8.5	101	10.2	0.1	6.0	4.6	36
	1-364	211	83	10.3	122	10.2	0.1	5.9	4.5	27
	1-365	155	54	8.5	107	10.1	0.2	6.1	4.7	38
6	2-366	105	51	7.1	105	9.8	0.1	6.2	4.6	30
	2-367	157	62	7.9	102	10.1	0.1	6.0	4.6	33
	2-368	120	44	6.5	131	10.0	0.1	5.9	4.5	40
	2-369	210	81	8.8	119	10.1	0.3	6.1	4.7	35
	2-370	204	106	9.0	117	9.9	0.2	6.1	4.7	31
1	3-371	134	52	7.0	104	9.7	0.1	5.6	4.2	27
	3-372	192	82	10.2	106	10.2	0.2	6.0	4.6	30
	3-373	136	53	7.1	118	9.6	0.2	5.8	4.3	24
	3-374	91	40	8.6	100	9.9	0.1	5.5	4.2	26
	3-375	140	53	8.1	113	9.9	0.2	5.8	4.5	33
0	4-376	180	78	9.5	96	10.1	0.2	5.7	4.4	28
	4-377	119	37	8.3	110	9.9	0.1	5.9	4.4	29
	4-378	140	41	7.3	84	9.7	0.1	5.9	4.3	27
	4-379	134	39	9.2	119	10.0	0.2	6.2	4.6	29
	4-380	157	52	8.7	116	9.9	0.2	5.8	4.6	36

## Clinical Chemistries/Females

90 Day

DOSE GROUPS	ANIMALS	GLUCOSE	BUN	CREAT	SODIUM	POTASSIUM	CHOL
(mg DNB/kg)							
diet	#	mg/dl	mg/dl	mg/dl	mmol/l	mmol/l	mg/dl
30	1-01	113	19	0.6	142	3.9	117
	1-02	120	19	0.5	143	4.7	121
	1-03	124	19	0.6	144	3.7	113
	1-04	114	22	0.5	142	4.2	108
	1-05	98	19	0.7	145	4.0	111
	1-06	125	17	0.5	*	*	53
	1-07	105	20	0.5	144	3.7	115
	1-08	95	20	0.6	143	4.3	112
	1-09	104	17	0.7	145	4.5	125
	1-10	112	22	0.6	144	4.6	103
6	2-11	114	15	0.6	143	4.2	115
	2-12	110	19	0.6	143	4.3	109
	2-13	92	18	0.6	143	4.1	119
	2-14	107	19	0.5	143	3.7	105
	2-15	113	19	0.5	144	3.9	105
	2-16	102	19	0.6	144	4.0	105
	2-17	120	15	0.6	141	3.7	112
	2-18	108	16	0.6	146	3.9	111
	2-19	97	18	0.5	144	4.6	99
	2-20	121	18	0.6	143	4.2	100
1	3-21	120	15	0.6	144	4.5	107
	3-22	104	15	0.5	143	3.9	97
	3-23	115	20	0.6	144	4.4	115
	3-24	106	20	0.6	142	3.9	111
	3-25	122	16	0.6	142	4.6	101
	3-26	130	19	0.7	143	4.4	125
	3-27	113	18	0.6	144	3.9	109
	3-28	106	18	0.6	143	4.7	106
	3-29	106	19	0.6	144	4.0	100
	3-30	129	19	0.6	143	4.4	93
0	4-31	109	20	0.6	144	3.7	99
	4-32	141	17	0.6	142	4.3	109
	4-33	125	15	0.6	142	3.8	103
	4-34	120	17	0.7	143	4.7	82
	4-35	131	20	0.6	144	4.1	103
	4-36	100	19	0.6	144	4.2	104
	4-37	126	16	0.5	141	4.5	110
	4-38	107	17	0.6	143	4.4	109
	4-39	112	17	0.5	143	4.2	115
	4-40	116	20	0.6	145	5.0	94

## Clinical Chemistries/Females

90 Day

DOSE GROUPS	ANIMALS	AST	ALT	PHOS	AP	Ca	TOTAL BILIRUBIN	TOTAL PROTEIN	ALB	TRIG
(mg DNB/kg) diet	#	U/L	U/L	mg/dl	U/L	mg/dl	mg/dl	g/dl	g/dl	mg/dl
30	1-01	148	57	8.8	69	10.0	0.1	6.5	4.6	33
	1-02	122	54	8.5	88	10.2	0.2	6.8	4.8	34
	1-03	133	67	7.9	77	9.9	0.1	6.6	4.4	44
	1-04	175	73	9.2	99	9.9	0.1	5.9	4.2	31
	1-05	148	56	8.9	75	9.4	0.1	5.8	4.2	20
	1-06	*	61	7.6	103	*	0.5	5.9	*	*
	1-07	145	59	8.3	82	9.6	0.1	6.2	4.6	42
	1-08	175	56	8.7	69	10.0	0.1	6.4	4.6	34
	1-09	155	82	9.2	63	10.1	0.1	6.7	4.8	40
	1-10	212	105	9.9	75	10.0	0.2	6.2	4.4	21
6	2-11	150	62	5.7	59	9.8	0.1	6.1	4.3	43
	2-12	183	58	8.0	75	10.1	0.2	6.3	4.4	36
	2-13	164	55	8.4	78	9.8	0.1	6.4	4.4	43
	2-14	150	52	7.8	81	9.5	0.1	6.1	4.4	32
	2-15	134	60	9.3	114	9.7	0.1	6.3	4.6	31
	2-16	214	104	7.6	80	9.7	0.1	6.2	4.3	31
	2-17	142	60	8.1	54	10.1	0.1	6.1	4.4	35
	2-18	190	61	5.5	57	9.9	0.1	6.0	4.3	36
	2-19	147	61	8.9	73	10.2	0.1	6.0	4.3	23
	2-20	176	67	7.7	60	9.7	0.1	5.7	4.0	46
1	3-21	132	55	7.1	65	9.9	0.1	6.4	4.6	35
	3-22	126	46	6.3	62	9.8	0.1	6.0	4.4	30
	3-23	153	57	7.9	89	9.7	0.2	6.5	4.4	29
	3-24	153	62	8.0	94	9.8	0.1	6.3	4.5	43
	3-25	146	69	7.1	74	9.9	0.1	5.7	4.0	48
	3-26	140	60	8.7	74	10.2	0.1	7.1	5.1	40
	3-27	148	69	5.6	71	10.0	0.1	6.6	4.6	34
	3-28	237	144	9.0	67	9.9	0.1	6.2	4.3	29
	3-29	201	118	9.1	99	9.6	0.2	5.9	4.2	34
	3-30	142	84	8.3	90	9.8	0.1	5.8	4.2	26
0	4-31	114	49	8.2	75	9.8	0.1	6.4	4.5	34
	4-32	126	63	7.3	90	9.9	0.1	5.6	4.0	28
	4-33	124	48	6.0	72	10.0	0.1	6.2	4.4	29
	4-34	215	87	9.7	76	9.8	0.1	6.1	4.3	25
	4-35	171	91	8.5	78	9.8	0.1	6.3	4.5	38
	4-36	157	62	8.7	92	9.8	0.1	6.2	4.3	26
	4-37	161	65	7.1	76	9.6	0.1	6.3	4.4	32
	4-38	182	87	6.9	58	9.8	0.1	5.9	4.3	39
	4-39	112	41	8.7	85	10.1	0.1	6.7	4.7	30
	4-40	137	61	8.5	85	9.7	0.1	6.3	4.4	30

Clinical Chemistries/Males  
45 Day

DOSE GROUPS (mg DNB/kg)	ANIMALS	GLUCOSE	BUN	CREAT	SODIUM	POTASSIUM	CHOL
diet	#	mg/dl	mg/dl	mg/dl	mmol/l	mmol/l	mg/dl
30	5-381	152	20	0.5	141	4.5	67
	5-382	176	20	0.6	141	4.8	58
	5-383	164	18	0.5	141	4.8	52
	5-384	169	21	0.6	141	4.8	58
	5-385	180	20	0.6	140	4.7	53
6	6-386	163	19	0.5	140	5.0	58
	6-387	169	23	0.6	152	5.1	58
	6-388	181	20	0.6	140	5.0	60
	6-389	204	22	0.6	141	4.7	51
	6-390	172	20	0.6	139	5.6	58
1	7-391	172	21	0.5	140	5.4	53
	7-392	183	21	0.6	141	5.5	55
	7-393	181	20	0.6	141	4.7	58
	7-394	172	21	0.5	140	4.8	53
	7-395	157	18	0.6	139	5.2	47
0	8-396	187	18	0.5	140	4.8	53
	8-397	135	17	0.5	139	5.2	58
	8-398	154	17	0.5	139	5.2	51
	8-399	160	16	0.5	140	5.4	53
	8-400	163	20	0.5	140	5.0	55

Clinical Chemistries/Males  
45 Day

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	AST U/L	ALT U/L	PHOS mg/dl	AP U/L	Ca mg/dl	TOTAL BILIRUBIN mg/dl	TOTAL PROTEIN g/dl	ALB g/dl	TRIG mg/dl
30	5-381	213	98	9.7	117	10.5	0.1	6.4	4.7	85
	5-382	209	96	9.2	125	10.5	0.1	6.5	4.8	144
	5-383	124	63	9.1	126	10.4	0.1	6.3	4.6	79
	5-384	148	78	9.1	105	10.3	0.1	6.2	4.6	55
	5-385	444	402	9.7	112	10.1	0.1	6.2	4.5	45
6	6-386	173	80	9.6	120	10.5	0.1	6.5	4.7	87
	6-387	148	61	9.4	140	10.5	0.1	6.9	4.9	126
	6-388	196	102	9.0	129	10.6	0.1	6.5	4.8	107
	6-389	367	313	8.9	129	10.3	0.2	6.2	4.7	140
	6-390	144	75	10.2	122	10.7	0.1	6.7	4.8	69
1	7-391	156	62	10.7	124	10.5	0.1	6.4	4.7	49
	7-392	137	62	9.6	131	10.5	0.1	6.3	4.5	106
	7-393	155	66	9.0	138	10.2	0.1	6.3	4.5	124
	7-394	153	68	9.4	123	10.1	0.1	5.8	4.5	106
	7-395	188	88	10.2	130	10.7	0.1	6.1	4.5	94
0	8-396	124	54	9.2	125	10.5	0.1	6.1	4.5	88
	8-397	149	74	9.7	101	10.3	0.1	6.2	4.5	70
	8-398	191	95	10.0	119	10.3	0.1	6.2	4.6	74
	8-399	141	67	9.9	117	10.5	0.1	6.2	4.4	53
	8-400	193	115	9.6	114	10.4	0.1	6.4	4.5	91

Clinical Chemistries/Males  
90 Day

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	GLUCOSE mg/dl	BUN mg/dl	CREAT mg/dl	SODIUM mmol/l	POTASSIUM mmol/l	CHOL mg/dl
30	5-41	187	19	0.6	142	4.3	81
	5-42	150	22	0.7	144	4.4	85
	5-43	170	19	0.6	143	4.5	82
	5-44	175	19	0.6	143	3.7	79
	5-45	182	19	0.7	144	4.5	72
	5-46	183	19	0.6	142	4.9	64
	5-47	155	17	0.6	143	4.8	68
	5-48	140	19	0.6	144	3.8	75
	5-49	156	14	0.6	143	4.8	68
	5-50	148	16	0.6	142	4.6	62
6	6-51	141	18	0.6	143	5.0	75
	6-52	144	16	0.6	142	4.4	77
	6-53	155	22	0.7	145	4.8	98
	6-54	161	19	0.6	143	5.2	79
	6-55	155	14	0.6	143	4.5	72
	6-56	141	23	0.7	144	4.7	91
	6-57	167	19	0.5	141	4.4	70
	6-58	157	16	0.6	143	4.7	82
	6-59	130	21	0.6	143	4.2	78
	6-60	147	21	0.6	144	4.2	74
1	7-61	161	21	0.6	144	4.6	89
	7-62	176	20	0.5	142	4.4	69
	7-63	149	21	0.6	143	4.6	72
	7-64	136	21	0.6	144	4.6	72
	7-65	133	16	0.6	142	4.1	62
	7-66	162	21	0.6	144	4.0	97
	7-67	162	21	0.6	143	4.3	77
	7-68	154	21	0.6	142	4.6	77
	7-69	137	24	0.7	143	4.2	70
	7-70	171	23	0.6	143	4.7	77
0	8-71	164	23	0.6	145	4.1	73
	8-72	177	22	0.6	143	5.0	83
	8-73	179	21	0.6	144	4.1	95
	8-74	163	18	0.6	143	4.4	70
	8-75	113	27	0.7	143	4.5	98
	8-76	149	20	0.6	143	5.0	70
	8-77	134	22	0.6	145	4.9	99
	8-78	149	22	0.6	144	4.2	67
	8-79	159	23	0.7	143	4.9	84
	8-80	165	19	0.6	145	4.7	77

Clinical Chemistries/Males  
90 Day

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	AST U/L	ALT U/L	PHOS mg/dl	AP U/L	Ca mg/dl	TOTAL BILIRUBIN mg/dl	TOTAL PROTEIN g/dl	ALB g/dl	TRIG mg/dl
30	5-41	169	105	8.5	82	10.1	0.1	6.4	4.5	102
	5-42	209	97	8.3	101	9.9	0.1	6.5	4.5	74
	5-43	345	185	8.4	86	10.2	0.1	6.5	4.7	69
	5-44	339	191	7.8	92	10.0	0.1	6.5	4.7	91
	5-45	251	146	8.5	94	10.0	0.1	6.4	4.5	71
	5-46	238	151	8.9	101	10.1	0.1	6.3	4.6	42
	5-47	135	62	7.6	72	10.0	0.1	6.1	4.4	24
	5-48	129	66	7.2	94	10.2	0.1	6.4	4.7	75
	5-49	151	66	8.5	77	9.9	0.1	6.3	4.5	38
	5-50	183	93	8.9	68	9.7	0.1	5.8	4.1	12
6	6-51	228	103	8.9	88	10.1	0.1	6.5	4.5	66
	6-52	148	69	8.9	69	10.2	0.1	6.4	4.4	43
	6-53	256	105	8.1	102	10.5	0.1	6.7	4.6	72
	6-54	301	163	8.6	91	10.4	0.1	6.8	4.6	66
	6-55	189	92	7.5	81	9.9	0.1	6.3	4.2	34
	6-56	269	148	9.0	95	10.4	0.1	6.6	4.6	82
	6-57	158	84	8.5	91	10.2	0.1	6.5	4.4	98
	6-58	168	77	7.9	69	10.0	0.1	6.2	4.4	36
	6-59	251	126	8.3	101	10.1	0.1	6.2	4.3	76
	6-60	221	101	7.6	115	10.2	0.1	6.6	4.6	119
1	7-61	235	103	7.3	101	10.3	0.1	6.8	4.5	99
	7-62	245	127	8.2	110	10.2	0.1	6.5	4.6	66
	7-63	239	101	8.4	99	10.2	0.1	6.7	4.8	83
	7-64	194	75	8.4	102	10.5	0.1	6.8	4.8	75
	7-65	192	86	7.5	88	9.9	0.1	6.5	4.5	28
	7-66	215	100	7.9	88	10.4	0.1	6.6	4.6	134
	7-67	176	96	7.9	107	10.2	0.1	6.3	4.4	132
	7-68	248	123	8.0	106	10.4	0.1	6.8	4.7	95
	7-69	204	108	7.4	116	10.2	0.1	6.4	4.6	116
	7-70	253	159	8.7	125	9.9	0.1	6.2	4.4	53
0	8-71	287	192	8.3	124	10.2	0.1	6.8	4.7	81
	8-72	271	148	8.9	115	10.2	0.1	6.6	4.6	108
	8-73	142	82	8.4	111	10.1	0.1	6.6	4.7	94
	8-74	177	89	8.0	80	10.0	0.0	6.4	4.4	31
	8-75	198	67	9.0	92	10.4	0.1	6.6	4.6	75
	8-76	264	123	8.6	102	10.5	0.1	6.8	4.6	60
	8-77	237	112	8.7	96	10.5	0.1	6.7	4.7	78
	8-78	239	125	7.7	97	9.9	0.1	6.2	4.3	81
	8-79	296	206	8.4	113	10.2	0.1	6.3	4.5	96
	8-80	244	117	7.4	94	10.2	0.1	6.5	4.7	91



APPENDIX F

CLINICAL OBSERVATIONS

DATE	CLINICAL OBSERVATIONS
08/23/94	Study started today for the females. All animals look normal.
08/24/94	Study started today for the males. All animals look normal.
08/25/94	All animals look normal.
08/26/94	All animals look normal.
08/29/94	All animals look normal.
08/30/94	Some of the animals have small skin lesions at the site of injection of ID implant. All other animals look normal.
08/31/94	All animals look normal.
09/01/94	All animals look normal.
09/02/94	All animals look normal.
09/06/94	All animals look normal.
09/07/94	All animals look normal.
09/09/94	All animals look normal.
09/12/94	All animals look normal.
09/13/94	All animals look normal.
09/14/94	All animals look normal.
09/15/94	All animals look normal.
09/16/94	All animals look normal.
09/19/94	All animals look normal.
09/20/94	All animals look normal.
09/21/94	All animals look normal.
09/22/94	All animals look normal.
09/23/94	All animals look normal.
09/26/94	All animals look normal.
09/27/94	All animals look normal.
09/28/94	All animals look normal.
09/29/94	All animals look normal.
09/30/94	All animals look normal.
10/04/94	All animals look normal.
10/05/94	All animals look normal.
10/06/94	All animals look normal.
10/07/94	All animals look normal.
10/11/94	All animals look normal.
10/12/94	All animals look normal.
10/13/94	All animals look normal.
10/14/94	All animals look normal.
10/17/94	All animals look normal.
10/18/94	All animals look normal.
10/19/94	All animals look normal.
10/20/94	All animals look normal.
10/24/94	All animals look normal.
10/25/94	All animals look normal.

DATE	CLINICAL OBSERVATIONS
10/26/94	All animals look normal.
10/27/94	All animals look normal.
10/28/94	All animals look normal.
10/31/94	All animals look normal.
11/01/94	All animals look normal.
11/02/94	All animals look normal.
11/03/94	All animals look normal.
11/04/94	All animals look normal.
11/08/94	All animals look normal.
11/09/94	All animals look normal.
11/10/94	All animals look normal.
11/11/94	All animals look normal.
11/14/94	All animals look normal.
11/15/94	All animals look normal.
11/16/94	All animals look normal.
11/17/94	All animals look normal.
11/18/94	All animals look normal.
11/21/94	Eye exams were performed today. 40 females and 10 males were fasted in the afternoon. All animals look normal.
11/22/94	40 males and 10 females were removed for necropsy. The remaining 30 females were fasted in the afternoon. All animals look normal.
11/23/94	The final 30 males were necropsied today.

APPENDIX G  
OPHTHALMOLOGY DATA

## Ophthalmology Report

David A. Wilkie DVM, MS  
Diplomate ACVO

### Introduction

The following are results of ocular examinations. All ocular examinations were performed by a Board-Certified Veterinary Ophthalmologist.

### Materials and Methods

An final ophthalmic examination was performed on the eyes of all rats by Dr David Wilkie DVM, MS, Dip. ACVO prior to completion of the study. Examinations included:

1. Biomicroscopic examination, using a Zeiss HSO-10 biomicroscope, following dilation of the pupils with 1.0% tropicamide (Mydracil®).
2. Indirect ophthalmoscopic examination, using a 30 diopter lens, following dilation of the pupils with 1.0% tropicamide (Mydracil®).

### Results

#### Final Examination

Corneal dystrophy (crystals) -

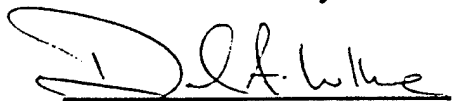
The eyes of all animals examined were affected by corneal dystrophy/crystals. All animals were affected with mild corneal dystrophy OU.

Conjunctivitis OU -

Animal # 44 affected with mild conjunctivitis.

### Conclusions

All animals used in this study were affected with mild corneal dystrophy prior to the initiation of the study. Corneal dystrophy is a common finding in Fisher 344 rats of both sexes. Progression of the corneal dystrophy was not observed to occur and the dystrophy did not interfere with ophthalmic examination in this study. Conjunctivitis was observed in a single animal and is unassociated with treatment. There was no treatment-related ophthalmic effect observed in the animals on this study.



Date: 11/27/94

David A. Wilkie DVM, MS  
Diplomate ACVO  
Associate Professor  
Department of Veterinary Clinical Sciences  
The Ohio State University  
601 Vernon L. Tharp Street  
Columbus, Ohio 43210

## Ophthalmology Report

David A. Wilkie DVM, MS  
Diplomate ACVO

### Introduction

The following are results of ocular examinations. All ocular examinations were performed by a Board-Certified Veterinary Ophthalmologist.

### Materials and Methods

An initial ophthalmic examination was performed on the eyes of all rats by Dr David Wilkie DVM, MS, Dip. ACVO prior to initiation of the study. Examinations included:

1. Biomicroscopic examination, using a Zeiss HSO-10 biomicroscope, following dilation of the pupils with 1.0% tropicamide (Mydracyl®).
2. Indirect ophthalmoscopic examination, using a 30 diopter lens, following dilation of the pupils with 1.0% tropicamide (Mydracyl®).

### Results

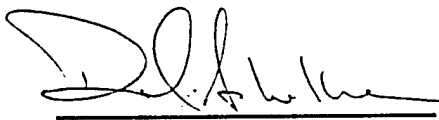
#### Initial Examination

Corneal dystrophy (crystals) -

The eyes of all animals examined were affected by corneal dystrophy/crystals. All animals were affected with mild corneal dystrophy OU.

### Conclusions

All animals to be used in this study are affected with mild corneal dystrophy prior to the initiation of the study. Corneal dystrophy is a common finding in Fisher 344 rats of both sexes. Progression of the corneal dystrophy will occur, but should not interfere with ophthalmic examination in a study of this length.



Date: 8/12/94

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APPENDIX H

GROSS AND  
HISTOPATHOLOGY  
DATA

## REPORTS CODE TABLE

N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
U	Tissues unavailable/unsuitable for evaluation
*	Tissues not examined/not required by protocol
1	Minimal
2	Mild
3	Moderate
4	Marked

### Abbreviation List

NOS

Not Otherwise Specified

(End of Report)



Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

## PROJECT SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
NUMBER OF ANIMALS:	10	10	10	10
	# %	# %	# %	# %
BRAIN	# EX 10	1	0	10
Astrocytoma	0 0.0	1 100.0	0 0.0	0 0.0
SCIATIC NERVE	# EX 10	0	0	10
SPINAL CORD	# EX 10	0	0	10
SALIVARY GLAND	# EX 10	0	0	10
PANCREAS	# EX 10	0	0	10
MANDIBULAR LYMPH NODE	# EX 10	0	0	10
Plasmacytosis	1 10.0	0 0.0	0 0.0	0 0.0
Inflammation, Chronic	0 0.0	0 0.0	0 0.0	1 10.0
Hyperplasia, Lymphoid	0 0.0	0 0.0	0 0.0	1 10.0
ZYMBAL'S GLAND	# EX 10	0	0	10
PITUITARY	# EX 10	0	0	10
ADRENALS	# EX 10	0	0	10
THYROID	# EX 10	0	0	10
PARATHYROID	# EX 10	0	0	10
TRACHEA	# EX 10	0	0	10
ESOPHAGUS	# EX 10	0	0	10

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
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## PROJECT SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1		2		3		4	
NUMBER OF ANIMALS:	10		10		10		10	
	#	%	#	%	#	%	#	%
THYMUS	# EX	10	0		0		10	
Hemorrhage		0 0.0	0 0.0		0 0.0		1 10.0	
HEART	# EX	10	0		0		10	
Inflammation, Chronic		2 20.0	0 0.0		0 0.0		1 10.0	
COLON	# EX	10	0		0		10	
JEJUNUM	# EX	10	0		0		10	
AORTA	# EX	10	0		0		10	
LIVER	# EX	10	0		0		10	
Inflammation, Chronic		1 10.0	0 0.0		0 0.0		0 0.0	
Hepatodiaphragmatic Nodule		0 0.0	0 0.0		0 0.0		1 10.0	
SPLEEN	# EX	10	10		10		10	
Hyperplasia, Erythroid Cell		8 80.0	0 0.0		0 0.0		0 0.0	
Pigmentation, NOS		9 90.0	1 10.0		3 30.0		0 0.0	
TONGUE	# EX	10	0		0		10	
SKELETAL MUSCLE	# EX	10	0		0		10	
LUNGS	# EX	10	0		0		10	
Inflammation, Chronic		1 10.0	0 0.0		0 0.0		0 0.0	
KIDNEY	# EX	10	10		10		10	
Lymphocytic Infiltrates		0 0.0	0 0.0		1 10.0		0 0.0	
Pigmentation, NOS		10 100.0	0 0.0		0 0.0		3 30.0	
Hyaline Droplets		9 90.0	0 0.0		0 0.0		0 0.0	

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
NUMBER OF ANIMALS:	10	10	10	10
	# %	# %	# %	# %
KIDNEY	# EX 10	10	10	10
Mineralization, NOS	10 100.0	10 100.0	10 100.0	9 90.0
URINARY BLADDER	# EX 10	0	0	10
STOMACH	# EX 10	0	0	10
DUODENUM	# EX 10	0	0	10
ILEUM	# EX 10	0	0	10
CECUM	# EX 10	0	0	10
RECTUM	# EX 10	0	0	10
MESENTERIC LYMPH NODE	# EX 10	0	0	10
Inflammation, Chronic	2 20.0	0 0.0	0 0.0	3 30.0
Hyperplasia, Lymphoid	1 10.0	0 0.0	0 0.0	0 0.0
OVARIES	# EX 10	0	2	10
Cyst, NOS	0 0.0	0 0.0	1 50.0	0 0.0
Inflammation, Chronic/Active, Parovarian	0 0.0	0 0.0	1 50.0	0 0.0
Necrosis, Parovarian	0 0.0	0 0.0	1 50.0	0 0.0
Bursal Cyst	0 0.0	0 0.0	0 0.0	1 10.0
UTERUS	# EX 10	0	0	10
Dilatation, Bilateral	4 40.0	0 0.0	0 0.0	2 20.0
SKIN	# EX 10	0	0	10

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
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## PROJECT SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1	2	3	4
NUMBER OF ANIMALS:		10	10	10	10
	# %	# %	# %	# %	# %
CLITORAL GLAND	# EX 10	0	0	10	
Lymphocytic Infiltrates	6 60.0	0 0.0	0 0.0	4 40.0	
Inflammation, Suppurative	1 10.0	0 0.0	0 0.0	0 0.0	
Inflammation, Chronic/Active	1 10.0	0 0.0	0 0.0	0 0.0	
EYES	# EX 10	0	0	10	
Microgranuloma, Cornea	4 40.0	0 0.0	0 0.0	2 20.0	
HARDERIAN GLAND	# EX 10	0	0	10	
Lymphocytic Infiltrates	4 40.0	0 0.0	0 0.0	2 20.0	
FEMUR/STERNUM	# EX 10	0	0	10	
Hyperplasia, Erythroid Cell	2 20.0	0 0.0	0 0.0	0 0.0	
NASAL	# EX 10	0	0	10	
MAMMARY GLAND	# EX 10	0	0	10	

Incidence Calculated by No. of Tissues Scored

(Report Continued)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

## PROJECT SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	5		6		7		8	
NUMBER OF ANIMALS:	10		10		10		10	
	#	%	#	%	#	%	#	%
BRAIN	# EX 10		0		0		10	
SCIATIC NERVE	# EX 10		0		0		10	
SPINAL CORD	# EX 10		0		0		10	
SALIVARY GLAND	# EX 10		0		0		10	
PANCREAS	# EX 10		0		0		10	
Degeneration, Acinar	0	0.0	0	0.0	0	0.0	2	20.0
MANDIBULAR LYMPH NODE	# EX 10		0		0		10	
Plasmacytosis	3	30.0	0	0.0	0	0.0	3	30.0
Hyperplasia, Lymphoid	1	10.0	0	0.0	0	0.0	1	10.0
ZYMBAL'S GLAND	# EX 8		0		0		9	
PITUITARY	# EX 10		0		0		10	
ADRENALS	# EX 10		0		0		10	
THYROID	# EX 10		0		0		10	
PARATHYROID	# EX 10		0		0		9	
TRACHEA	# EX 10		0		0		10	
ESOPHAGUS	# EX 10		0		0		10	
THYMUS	# EX 10		1		2		10	
Hemorrhage	0	0.0	1	100.0	2	100.0	2	20.0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		5	6	7	8
NUMBER OF ANIMALS:		10	10	10	10
		# %	# %	# %	# %
HEART	# EX	10	0	0	10
Inflammation, Chronic		4 40.0	0 0.0	0 0.0	4 40.0
COLON	# EX	10	0	0	10
JEJUNUM	# EX	10	0	0	10
AORTA	# EX	10	0	0	10
LIVER	# EX	10	0	0	10
Lymphocytic Infiltrates		1 10.0	0 0.0	0 0.0	1 10.0
Inflammation, Chronic		0 0.0	0 0.0	0 0.0	1 10.0
Inflammation, Chronic/Active		1 10.0	0 0.0	0 0.0	0 0.0
Hepatodiaphragmatic Nodule		0 0.0	0 0.0	0 0.0	1 10.0
SPLEEN	# EX	10	10	10	10
Fibrosis		0 0.0	0 0.0	0 0.0	1 10.0
Hyperplasia, Lymphocytic		0 0.0	0 0.0	0 0.0	1 10.0
Hyperplasia, Erythroid Cell		8 80.0	0 0.0	0 0.0	0 0.0
Pigmentation, NOS		10 100.0	0 0.0	0 0.0	0 0.0
TONGUE	# EX	10	0	0	10
SKELETAL MUSCLE	# EX	10	0	0	10
LUNGS	# EX	10	0	0	10
Inflammation, Chronic		2 20.0	0 0.0	0 0.0	6 60.0
KIDNEY	# EX	10	10	10	10
Regeneration, Tubular		10 100.0	10 100.0	10 100.0	10 100.0
Degeneration, Tubular		10 100.0	10 100.0	10 100.0	10 100.0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

## PROJECT SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	5	6	7	8
NUMBER OF ANIMALS:	10	10	10	10
	# %	# %	# %	# %
KIDNEY	# EX 10	10	10	10
Cytoplasmic Droplets	10 100.0	0 0.0	0 0.0	0 0.0
Mineralization, NOS	10 100.0	10 100.0	10 100.0	10 100.0
Hyaline Casts	1 10.0	0 0.0	0 0.0	0 0.0
URINARY BLADDER	# EX 10	0	0	9
Urolith, NOS	0 0.0	0 0.0	0 0.0	2 22.0
PROSTATE	# EX 10	0	0	9
Inflammation, Suppurative	1 10.0	0 0.0	0 0.0	0 0.0
Inflammation, Chronic/Active	0 0.0	0 0.0	0 0.0	1 11.0
STOMACH	# EX 10	0	0	10
DUODENUM	# EX 10	0	0	10
ILEUM	# EX 10	0	0	10
CECUM	# EX 10	0	0	10
RECTUM	# EX 10	0	0	10
MESENTERIC LYMPH NODE	# EX 10	0	0	10
Inflammation, Chronic	0 0.0	0 0.0	0 0.0	1 10.0
Inflammation, Chronic/Active, Mesentery	0 0.0	0 0.0	0 0.0	1 10.0
TESTES	# EX 10	10	10	10
Degeneration, Seminiferous Tubule	10 100.0	0 0.0	0 0.0	0 0.0
EPIDIDYIMIDES	# EX 10	0	0	10
Hypospermia	10 100.0	0 0.0	0 0.0	0 0.0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

## PROJECT SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	5		6		7		8	
NUMBER OF ANIMALS:	10		10		10		10	
	#	%	#	%	#	%	#	%
SEMINAL VESICLE	# EX 10		0		0		10	
SKIN	# EX 10		0		0		10	
PREPUTIAL GLAND	# EX 10		0		0		10	
Inflammation, Chronic/Active	3	30.0	0	0.0	0	0.0	4	40.0
Inflammation, Suppurative	0	0.0	0	0.0	0	0.0	1	10.0
Lymphocytic Infiltrates	5	50.0	0	0.0	0	0.0	8	80.0
EYES	# EX 10		0		0		10	
Microgranuloma, Cornea	7	70.0	0	0.0	0	0.0	5	50.0
HARDERIAN GLAND	# EX 10		0		0		10	
FEMUR/STERNUM	# EX 10		0		0		10	
Hyperplasia, Erythroid Cell	5	50.0	0	0.0	0	0.0	0	0.0
NASAL	# EX 10		0		0		10	
MAMMARY GLAND	# EX 10		0		0		10	

Incidence Calculated by No. of Tissues Scored

(End of Report)



Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4
NUMBER OF ANIMALS:	10	10	10	10
	# SEV	# SEV	# SEV	# SEV
BRAIN	# EX 10	1	0	10
SCIATIC NERVE	# EX 10	0	0	10
SPINAL CORD	# EX 10	0	0	10
SALIVARY GLAND	# EX 10	0	0	10
PANCREAS	# EX 10	0	0	10
MANDIBULAR LYMPH NODE	# EX 10	0	0	10
Plasmacytosis	1 0.20	0 0.00	0 0.00	0 0.00
Inflammation, Chronic	0 0.00	0 0.00	0 0.00	1 0.20
Hyperplasia, Lymphoid	0 0.00	0 0.00	0 0.00	1 0.10
ZYMBAL'S GLAND	# EX 10	0	0	10
PITUITARY	# EX 10	0	0	10
ADRENALS	# EX 10	0	0	10
THYROID	# EX 10	0	0	10
PARATHYROID	# EX 10	0	0	10
TRACHEA	# EX 10	0	0	10
ESOPHAGUS	# EX 10	0	0	10
THYMUS	# EX 10	0	0	10
Hemorrhage	0 0.00	0 0.00	0 0.00	1 0.10

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4
NUMBER OF ANIMALS:	10	10	10	10
	# SEV	# SEV	# SEV	# SEV
HEART	# EX 10	0	0	10
Inflammation, Chronic	2 0.20	0 0.00	0 0.00	1 0.10
COLON	# EX 10	0	0	10
JEJUNUM	# EX 10	0	0	10
AORTA	# EX 10	0	0	10
LIVER	# EX 10	0	0	10
Inflammation, Chronic	1 0.10	0 0.00	0 0.00	0 0.00
SPLEEN	# EX 10	10	10	10
Hyperplasia, Erythroid Cell	8 1.40	0 0.00	0 0.00	0 0.00
Pigmentation, NOS	9 1.10	1 0.10	3 0.30	0 0.00
TONGUE	# EX 10	0	0	10
SKELETAL MUSCLE	# EX 10	0	0	10
LUNGS	# EX 10	0	0	10
Inflammation, Chronic	1 0.10	0 0.00	0 0.00	0 0.00
KIDNEY	# EX 10	10	10	10
Lymphocytic Infiltrates	0 0.00	0 0.00	1 0.10	0 0.00
Pigmentation, NOS	10 1.00	0 0.00	0 0.00	3 0.30
Hyaline Droplets	9 1.10	0 0.00	0 0.00	0 0.00
Mineralization, NOS	10 1.00	10 1.20	10 1.30	9 0.90
URINARY BLADDER	# EX 10	0	0	10

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
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90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4
NUMBER OF ANIMALS:	10	10	10	10
	# SEV	# SEV	# SEV	# SEV
STOMACH	# EX 10 0	0	0	10
DUODENUM	# EX 10 0	0	0	10
ILEUM	# EX 10 0	0	0	10
CECUM	# EX 10 0	0	0	10
RECTUM	# EX 10 0	0	0	10
MESENTERIC LYMPH NODE	# EX 10 0	0	0	10
Inflammation, Chronic	2 0.30	0 0.00	0 0.00	3 0.40
Hyperplasia, Lymphoid	1 0.20	0 0.00	0 0.00	0 0.00
OVARIES	# EX 10 0	0	2	10
Inflammation, Chronic/Active, Parovarian	0 0.00	0 0.00	1 2.00	0 0.00
Necrosis, Parovarian	0 0.00	0 0.00	1 1.50	0 0.00
UTERUS	# EX 10 0	0	0	10
Dilatation, Bilateral	4 1.00	0 0.00	0 0.00	2 0.20
SKIN	# EX 10 0	0	0	10
CLITORAL GLAND	# EX 10 0	0	0	10
Lymphocytic Infiltrates	6 0.60	0 0.00	0 0.00	4 0.40
Inflammation, Suppurative	1 0.10	0 0.00	0 0.00	0 0.00
Inflammation, Chronic/Active	1 0.20	0 0.00	0 0.00	0 0.00
EYES	# EX 10 0	0	0	10
Microgranuloma, Cornea	4 0.40	0 0.00	0 0.00	2 0.20

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4
NUMBER OF ANIMALS:	10	10	10	10
HARDERIAN GLAND	# SEV	# SEV	# SEV	# SEV
# EX 10	0	0	10	
Lymphocytic Infiltrates	4 0.50	0 0.00	0 0.00	2 0.20
FEMUR/STERNUM	# EX 10	0	0	10
Hyperplasia, Erythroid Cell	2 0.30	0 0.00	0 0.00	0 0.00
NASAL	# EX 10	0	0	10
MAMMARY GLAND	# EX 10	0	0	10

Severity Calculated by No. of Tissues Scored

(Report Continued)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

### SEVERITY SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	5	6	7	8
NUMBER OF ANIMALS:	10	10	10	10
	# SEV	# SEV	# SEV	# SEV
BRAIN	# EX 10	0	0	10
SCIATIC NERVE	# EX 10	0	0	10
SPINAL CORD	# EX 10	0	0	10
SALIVARY GLAND	# EX 10	0	0	10
PANCREAS	# EX 10	0	0	10
Degeneration, Acinar	0 0.00	0 0.00	0 0.00	2 0.20
MANDIBULAR LYMPH NODE	# EX 10	0	0	10
Plasmacytosis	3 0.50	0 0.00	0 0.00	3 0.60
Hyperplasia, Lymphoid	1 0.20	0 0.00	0 0.00	1 0.20
ZYMBAL'S GLAND	# EX 8	0	0	9
PITUITARY	# EX 10	0	0	10
ADRENALS	# EX 10	0	0	10
THYROID	# EX 10	0	0	10
PARATHYROID	# EX 10	0	0	9
TRACHEA	# EX 10	0	0	10
ESOPHAGUS	# EX 10	0	0	10
THYMUS	# EX 10	1	2	10
Hemorrhage	0 0.00	1 2.00	2 2.50	2 0.30

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

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## SEVERITY SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	5	6	7	8
NUMBER OF ANIMALS:	10	10	10	10
	# SEV	# SEV	# SEV	# SEV
HEART	# EX 10	0	0	10
Inflammation, Chronic	4 0.50	0 0.00	0 0.00	4 0.40
COLON	# EX 10	0	0	10
JEJUNUM	# EX 10	0	0	10
AORTA	# EX 10	0	0	10
LIVER	# EX 10	0	0	10
Lymphocytic Infiltrates	1 0.10	0 0.00	0 0.00	1 0.10
Inflammation, Chronic	0 0.00	0 0.00	0 0.00	1 0.10
Inflammation, Chronic/Active	1 0.10	0 0.00	0 0.00	0 0.00
SPLEEN	# EX 10	10	10	10
Fibrosis	0 0.00	0 0.00	0 0.00	1 0.10
Hyperplasia, Lymphocytic	0 0.00	0 0.00	0 0.00	1 0.20
Hyperplasia, Erythroid Cell	8 1.30	0 0.00	0 0.00	0 0.00
Pigmentation, NOS	10 1.30	0 0.00	0 0.00	0 0.00
TONGUE	# EX 10	0	0	10
SKELETAL MUSCLE	# EX 10	0	0	10
LUNGS	# EX 10	0	0	10
Inflammation, Chronic	2 0.20	0 0.00	0 0.00	6 0.60
KIDNEY	# EX 10	10	10	10
Regeneration, Tubular	10 1.50	10 1.60	10 1.80	10 1.40
Degeneration, Tubular	10 1.80	10 2.00	10 2.00	10 1.80
Cytoplasmic Droplets	10 1.70	0 0.00	0 0.00	0 0.00
Mineralization, NOS	10 1.80	10 1.70	10 1.50	10 1.50

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	5	6	7	8
NUMBER OF ANIMALS:	10	10	10	10
	# SEV	# SEV	# SEV	# SEV
KIDNEY	# EX 10	10	10	10
Hyaline Casts	1 0.10	0 0.00	0 0.00	0 0.00
URINARY BLADDER	# EX 10	0	0	9
PROSTATE	# EX 10	0	0	9
Inflammation, Suppurative	1 0.20	0 0.00	0 0.00	0 0.00
Inflammation, Chronic/Active	0 0.00	0 0.00	0 0.00	1 0.22
STOMACH	# EX 10	0	0	10
DUODENUM	# EX 10	0	0	10
ILEUM	# EX 10	0	0	10
CECUM	# EX 10	0	0	10
RECTUM	# EX 10	0	0	10
MESENTERIC LYMPH NODE	# EX 10	0	0	10
Inflammation, Chronic	0 0.00	0 0.00	0 0.00	1 0.20
Inflammation, Chronic/Active, Mesentery	0 0.00	0 0.00	0 0.00	1 0.20
TESTES	# EX 10	10	10	10
Degeneration, Seminiferous Tubule	10 4.00	0 0.00	0 0.00	0 0.00
EPIDIDYMIDES	# EX 10	0	0	10
Hypospermia	10 4.00	0 0.00	0 0.00	0 0.00
SEMINAL VESICLE	# EX 10	0	0	10

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	5	6	7	8
NUMBER OF ANIMALS:	10	10	10	10
	# SEV	# SEV	# SEV	# SEV
SKIN	# EX 10	0	0	10
PREPUTIAL GLAND	# EX 10	0	0	10
Inflammation, Chronic/Active	3 0.80	0 0.00	0 0.00	4 0.90
Inflammation, Suppurative	0 0.00	0 0.00	0 0.00	1 0.30
Lymphocytic Infiltrates	5 0.50	0 0.00	0 0.00	8 1.30
EYES	# EX 10	0	0	10
Microgranuloma, Cornea	7 1.10	0 0.00	0 0.00	5 0.80
HARDERIAN GLAND	# EX 10	0	0	10
FEMUR/STERNUM	# EX 10	0	0	10
Hyperplasia, Erythroid Cell	5 0.80	0 0.00	0 0.00	0 0.00
NASAL	# EX 10	0	0	10
MAMMARY GLAND	# EX 10	0	0	10

Severity Calculated by No. of Tissues Scored

(END OF REPORT)



Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

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STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 1

DAYS ON TEST: ALL

SEX: FEMALE

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ANIMAL ID:	1-01	1-02	1-03	1-04	1-05	1-06	1-07	1-08	1-09	1-10
BRAIN	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N	N	N	N		N
Plasmacytosis	-	-	-	-	-	-	-	-	2	-
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N
PITUITARY	N	N	N	N	N	N	N	N	N	N
ADRENALS	N	N	N	N	N	N	N	N	N	N
THYROID	N	N	N	N	N	N	N	N	N	N
PARATHYROID	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	N	N	N
HEART		N	N	N	N	N	N	N		N

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-004

GROUP: 1

SEX: FEMALE

---

ANIMAL ID:	1-01	1-02	1-03	1-04	1-05	1-06	1-07	1-08	1-09	1-10
HEART		N	N	N	N	N	N	N		N
Inflammation, Chronic	1	-	-	-	-	-	-	-	1	-
COLON	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
LIVER	N		N	N	N	N	N	N	N	N
Inflammation, Chronic	-	1	-	-	-	-	-	-	-	-
SPLEEN						N				
Hyperplasia, Erythroid Cell	2	2	1	-	2	-	2	2	1	2
Pigmentation, NOS	1	2	1	1	1	-	2	1	1	1
TONGUE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNGS		N	N	N	N	N	N	N	N	N
Inflammation, Chronic	1	-	-	-	-	-	-	-	-	-
KIDNEY										
Pigmentation, NOS	1	1	1	1	1	1	1	1	1	1
Hyaline Droplets	2	1	1	-	1	1	2	1	1	1
Mineralization, NOS	1	1	1	1	1	1	1	1	1	1
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 1

DAYS ON TEST: ALL

SEX: FEMALE

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ANIMAL ID:	1-01	1-02	1-03	1-04	1-05	1-06	1-07	1-08	1-09	1-10
DUODENUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE		N	N	N	N	N	N	N		N
Inflammation, Chronic	1	-	-	-	-	-	-	-	2	-
Hyperplasia, Lymphoid	-	-	-	-	-	-	-	-	2	-
OVARIES	N	N	N	N	N	N	N	N	N	N
UTERUS	N	N	N			N	N			N
Dilatation, Bilateral	-	-	-	4	1	-	-	3	2	-
SKIN	N	N	N	N	N	N	N	N	N	N
CLITORAL GLAND	N					N				
Lymphocytic Infiltrates	-	1	1	1	-	-	-	1	1	1
Inflammation, Suppurative	-	-	-	-	-	-	1	-	-	-
Inflammation, Chronic/Active	-	-	-	-	2	-	-	-	-	-
EYES	N		N	N	N			N	N	
Microgranuloma, Cornea	-	1	-	-	-	1	1	-	-	1
HARDERIAN GLAND	N	N				N	N		N	N
Lymphocytic Infiltrates	-	-	2	1	1	-	-	1	-	-
FEMUR/STERNUM		N	N	N	N	N	N		N	N
Hyperplasia, Erythroid Cell	2	-	-	-	-	-	-	1	-	-

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 1

DAYS ON TEST: ALL

SEX: FEMALE

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ANIMAL ID:	1-01	1-02	1-03	1-04	1-05	1-06	1-07	1-08	1-09	1-10
NASAL	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 2

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	2-11	2-12	2-13	2-14	2-15	2-16	2-17	2-18	2-19	2-20
BRAIN	*	*	*		*	*	*	*	*	*
Astrocytoma	-	-	-	P	-	-	-	-	-	-
SCIATIC NERVE	*	*	*	*	*	*	*	*	*	*
SPINAL CORD	*	*	*	*	*	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*	*	*	*	*	*
PANCREAS	*	*	*	*	*	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*	*	*	*	*	*
PITUITARY	*	*	*	*	*	*	*	*	*	*
ADRENALS	*	*	*	*	*	*	*	*	*	*
THYROID	*	*	*	*	*	*	*	*	*	*
PARATHYROID	*	*	*	*	*	*	*	*	*	*
TRACHEA	*	*	*	*	*	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*	*	*	*	*	*
THYMUS	*	*	*	*	*	*	*	*	*	*
HEART	*	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 2

DAYS ON TEST: ALL

SEX: FEMALE

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ANIMAL ID:	2-11	2-12	2-13	2-14	2-15	2-16	2-17	2-18	2-19	2-20
JEJUNUM	*	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*	*
LIVER	*	*	*	*	*	*	*	*	*	*
SPLEEN	N	N		N	N	N	N	N	N	N
Pigmentation, NOS	-	-	1	-	-	-	-	-	-	-
TONGUE	*	*	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	*	*	*	*
LUNGS	*	*	*	*	*	*	*	*	*	*
KIDNEY										
Mineralization, NOS	1	1	1	1	1	2	1	1	2	1
URINARY BLADDER	*	*	*	*	*	*	*	*	*	*
STOMACH	*	*	*	*	*	*	*	*	*	*
DUODENUM	*	*	*	*	*	*	*	*	*	*
ILEUM	*	*	*	*	*	*	*	*	*	*
CECUM	*	*	*	*	*	*	*	*	*	*
RECTUM	*	*	*	*	*	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*	*	*	*	*	*

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA  
-----

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 2

DAYS ON TEST: ALL

SEX: FEMALE  
-----

ANIMAL ID:	2-11	2-12	2-13	2-14	2-15	2-16	2-17	2-18	2-19	2-20
OVARIES	*	*	*	*	*	*	*	*	*	*
UTERUS	*	*	*	*	*	*	*	*	*	*
SKIN	*	*	*	*	*	*	*	*	*	*
CLITORAL GLAND	*	*	*	*	*	*	*	*	*	*
EYES	*	*	*	*	*	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*	*	*	*	*	*
NASAL	*	*	*	*	*	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*	*	*	*	*	*

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 3

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	3-21	3-22	3-23	3-24	3-25	3-26	3-27	3-28	3-29	3-30
BRAIN	*	*	*	*	*	*	*	*	*	*
SCIATIC NERVE	*	*	*	*	*	*	*	*	*	*
SPINAL CORD	*	*	*	*	*	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*	*	*	*	*	*
PANCREAS	*	*	*	*	*	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*	*	*	*	*	*
PITUITARY	*	*	*	*	*	*	*	*	*	*
ADRENALS	*	*	*	*	*	*	*	*	*	*
THYROID	*	*	*	*	*	*	*	*	*	*
PARATHYROID	*	*	*	*	*	*	*	*	*	*
TRACHEA	*	*	*	*	*	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*	*	*	*	*	*
THYMUS	*	*	*	*	*	*	*	*	*	*
HEART	*	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)



Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 3

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	3-21	3-22	3-23	3-24	3-25	3-26	3-27	3-28	3-29	3-30
JEJUNUM	*	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*	*
LIVER	*	*	*	*	*	*	*	*	*	*
SPLEEN		N	N	N	N			N	N	N
Pigmentation, NOS	1	-	-	-	-	1	1	-	-	-
TONGUE	*	*	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	*	*	*	*
LUNGS	*	*	*	*	*	*	*	*	*	*
KIDNEY										
Lymphocytic Infiltrates	-	-	1	-	-	-	-	-	-	-
Mineralization, NOS	2	1	1	1	1	2	1	1	2	1
URINARY BLADDER	*	*	*	*	*	*	*	*	*	*
STOMACH	*	*	*	*	*	*	*	*	*	*
DUODENUM	*	*	*	*	*	*	*	*	*	*
ILEUM	*	*	*	*	*	*	*	*	*	*
CECUM	*	*	*	*	*	*	*	*	*	*
RECTUM	*	*	*	*	*	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 3

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	3-21	3-22	3-23	3-24	3-25	3-26	3-27	3-28	3-29	3-30
OVARIES	*	*	*	*		*	*	*		*
Cyst, NOS	-	-	-	-	-	-	-	-	P	-
Inflammation, Chronic/Active, Parovarian	-	-	-	-	4	-	-	-	-	-
Necrosis, Parovarian	-	-	-	-	3	-	-	-	-	-
UTERUS	*	*	*	*	*	*	*	*	*	*
SKIN	*	*	*	*	*	*	*	*	*	*
CLITORAL GLAND	*	*	*	*	*	*	*	*	*	*
EYES	*	*	*	*	*	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*	*	*	*	*	*
NASAL	*	*	*	*	*	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 4

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	4-31	4-32	4-33	4-34	4-35	4-36	4-37	4-38	4-39	4-40
BRAIN	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
MANDIBULAR LYMPH NODE		N	N	N	N	N	N	N	N	N
Inflammation, Chronic	2	-	-	-	-	-	-	-	-	-
Hyperplasia, Lymphoid	1	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N
PITUITARY	N	N	N	N	N	N	N	N	N	N
ADRENALS	N	N	N	N	N	N	N	N	N	N
THYROID	N	N	N	N	N	N	N	N	N	N
PARATHYROID	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N		N	N	N
Hemorrhage	-	-	-	-	-	-	1	-	-	-
HEART	N	N	N	N	N	N	N	N		N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 4

DAYS ON TEST: ALL

SEX: FEMALE

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ANIMAL ID:	4-31	4-32	4-33	4-34	4-35	4-36	4-37	4-38	4-39	4-40
HEART	N	N	N	N	N	N	N	N		N
Inflammation, Chronic	-	-	-	-	-	-	-	-	1	-
COLON	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N		N	N	N	N	N	N
Hepatodiaphragmatic Nodule	-	-	-	P	-	-	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNGS	N	N	N	N	N	N	N	N	N	N
KIDNEY						N				
Pigmentation, NOS	-	1	-	1	-	-	1	-	-	-
Mineralization, NOS	1	1	1	1	1	-	1	1	1	1
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 4

DAYS ON TEST: ALL

SEX: FEMALE

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ANIMAL ID:	4-31	4-32	4-33	4-34	4-35	4-36	4-37	4-38	4-39	4-40
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE		N	N	N	N	N	N			N
Inflammation, Chronic	2	-	-	-	-	-	-	1	1	-
OVARIES	N	N	N		N	N	N	N	N	N
Bursal Cyst	-	-	-	P	-	-	-	-	-	-
UTERUS	N	N	N	N		N	N	N	N	
Dilatation, Bilateral	-	-	-	-	1	-	-	-	-	1
SKIN	N	N	N	N	N	N	N	N	N	N
CLITORAL GLAND		N	N	N		N		N		N
Lymphocytic Infiltrates	1	-	-	-	1	-	1	-	1	-
EYES	N		N	N	N	N	N	N		N
Microgranuloma, Cornea	-	1	-	-	-	-	-	-	1	-
HARDERIAN GLAND	N		N	N		N	N	N	N	N
Lymphocytic Infiltrates	-	1	-	-	1	-	-	-	-	-
FEMUR/STERNUM	N	N	N	N	N	N	N	N	N	N
NASAL	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 5

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	5-41	5-42	5-43	5-44	5-45	5-46	5-47	5-48	5-49	5-50
BRAIN	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
MANDIBULAR LYMPH NODE		N	N	N			N	N	N	
Plasmacytosis	2	-	-	-	2	1	-	-	-	-
Hyperplasia, Lymphoid	-	-	-	-	-	-	-	-	-	2
ZYMBAL'S GLAND	N	U	N	N	N	N	N	N	U	N
PITUITARY	N	N	N	N	N	N	N	N	N	N
ADRENALS	N	N	N	N	N	N	N	N	N	N
THYROID	N	N	N	N	N	N	N	N	N	N
PARATHYROID	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	N	N	N
HEART			N	N	N			N	N	N
Inflammation, Chronic	1	1	-	-	-	2	1	-	-	-

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 5

DAYS ON TEST: ALL

SEX: MALE

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ANIMAL ID:	5-41	5-42	5-43	5-44	5-45	5-46	5-47	5-48	5-49	5-50
COLON	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
LIVER	N		N		N	N	N	N	N	N
Lymphocytic Infiltrates	-	1	-	-	-	-	-	-	-	-
Inflammation, Chronic/Active	-	-	-	1	-	-	-	-	-	-
SPLEEN										
Hyperplasia, Erythroid Cell	2	-	2	2	1	2	1	2	1	-
Pigmentation, NOS	2	1	2	1	1	1	1	2	1	1
TONGUE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNGS		N	N	N	N	N	N	N		N
Inflammation, Chronic	1	-	-	-	-	-	-	-	1	-
KIDNEY										
Regeneration, Tubular	1	1	1	2	2	2	2	1	1	2
Degeneration, Tubular	3	2	2	2	2	2	1	1	1	2
Hyaline Droplets	2	2	2	2	2	2	1	1	1	2
Mineralization, NOS	2	2	2	2	2	2	2	1	1	2
Hyaline Casts	-	-	-	-	1	-	-	-	-	-
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
PROSTATE	N	N	N	N	N		N	N	N	N
Inflammation, Suppurative	-	-	-	-	-	2	-	-	-	-

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-004

GROUP: 5

SEX: MALE

---

ANIMAL ID:	5-41	5-42	5-43	5-44	5-45	5-46	5-47	5-48	5-49	5-50
STOMACH	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N	N	N	N	N	N
TESTES										
Degeneration, Seminiferous Tubule	4	4	4	4	4	4	4	4	4	4
EPIDIDYIMIDES										
Hypospermia	4	4	4	4	4	4	4	4	4	4
SEMINAL VESICLE	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
PREPUTIAL GLAND						N			N	
Inflammation, Chronic/Active	3	3	2	-	-	-	-	-	-	-
Lymphocytic Infiltrates	-	-	-	1	1	-	1	1	-	1
EYES	N		N	N						
Microgranuloma, Cornea	-	2	-	-	1	2	2	1	1	2
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
FEMUR/STERNUM					N	N	N	N	N	

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)



Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 5

DAYS ON TEST: ALL

SEX: MALE  
-----

ANIMAL ID:	5-41	5-42	5-43	5-44	5-45	5-46	5-47	5-48	5-49	5-50
FEMUR/STERNUM					N	N	N	N	N	
Hyperplasia, Erythroid Cell	2	1	2	2	-	-	-	-	-	1
NASAL	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 6

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	6-51	6-52	6-53	6-54	6-55	6-56	6-57	6-58	6-59	6-60
BRAIN	*	*	*	*	*	*	*	*	*	*
SCIATIC NERVE	*	*	*	*	*	*	*	*	*	*
SPINAL CORD	*	*	*	*	*	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*	*	*	*	*	*
PANCREAS	*	*	*	*	*	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*	*	*	*	*	*
PITUITARY	*	*	*	*	*	*	*	*	*	*
ADRENALS	*	*	*	*	*	*	*	*	*	*
THYROID	*	*	*	*	*	*	*	*	*	*
PARATHYROID	*	*	*	*	*	*	*	*	*	*
TRACHEA	*	*	*	*	*	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*	*	*	*	*	*
THYMUS	*	*	*	*	*	*	*	*	*	*
Hemorrhage	-	-	-	-	-	-	-	-	2	-
HEART	*	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

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STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 6

DAYS ON TEST: ALL

SEX: MALE

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ANIMAL ID:	6-51	6-52	6-53	6-54	6-55	6-56	6-57	6-58	6-59	6-60
JEJUNUM	*	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*	*
LIVER	*	*	*	*	*	*	*	*	*	*
SPLEEN	N	N	N	N	N	N	N	N	N	N
TONGUE	*	*	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	*	*	*	*
LUNGS	*	*	*	*	*	*	*	*	*	*
KIDNEY										
Regeneration, Tubular	1	2	2	1	1	2	1	2	2	2
Degeneration, Tubular	2	2	2	2	2	2	2	2	2	2
Mineralization, NOS	1	2	2	2	1	2	1	2	2	2
URINARY BLADDER	*	*	*	*	*	*	*	*	*	*
PROSTATE	*	*	*	*	*	*	*	*	*	*
STOMACH	*	*	*	*	*	*	*	*	*	*
DUODENUM	*	*	*	*	*	*	*	*	*	*
ILEUM	*	*	*	*	*	*	*	*	*	*
CECUM	*	*	*	*	*	*	*	*	*	*
RECTUM	*	*	*	*	*	*	*	*	*	*

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB  
 FATE: ALL  
 DAYS ON TEST: ALL

STUDY NUMBER: 94-004  
 GROUP: 6  
 SEX: MALE

ANIMAL ID:	6-51	6-52	6-53	6-54	6-55	6-56	6-57	6-58	6-59	6-60
MESENTERIC LYMPH NODE	*	*	*	*	*	*	*	*	*	*
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIDES	*	*	*	*	*	*	*	*	*	*
SEMINAL VESICLE	*	*	*	*	*	*	*	*	*	*
SKIN	*	*	*	*	*	*	*	*	*	*
PREPUTIAL GLAND	*	*	*	*	*	*	*	*	*	*
EYES	*	*	*	*	*	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*	*	*	*	*	*
NASAL	*	*	*	*	*	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 7

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	7-61	7-62	7-63	7-64	7-65	7-66	7-67	7-68	7-69	7-70
BRAIN	*	*	*	*	*	*	*	*	*	*
SCIATIC NERVE	*	*	*	*	*	*	*	*	*	*
SPINAL CORD	*	*	*	*	*	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*	*	*	*	*	*
PANCREAS	*	*	*	*	*	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*	*	*	*	*	*
PITUITARY	*	*	*	*	*	*	*	*	*	*
ADRENALS	*	*	*	*	*	*	*	*	*	*
THYROID	*	*	*	*	*	*	*	*	*	*
PARATHYROID	*	*	*	*	*	*	*	*	*	*
TRACHEA	*	*	*	*	*	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*	*	*	*	*	*
THYMUS	*	*	*	*	*		*	*		*
Hemorrhage	-	-	-	-	-	2	-	-	3	-
HEART	*	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 7

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	7-61	7-62	7-63	7-64	7-65	7-66	7-67	7-68	7-69	7-70
JEJUNUM	*	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*	*
LIVER	*	*	*	*	*	*	*	*	*	*
SPLEEN	N	N	N	N	N	N	N	N	N	N
TONGUE	*	*	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	*	*	*	*
LUNGS	*	*	*	*	*	*	*	*	*	*
KIDNEY										
Regeneration, Tubular	2	2	1	2	1	2	2	2	2	2
Degeneration, Tubular	2	2	2	2	2	2	2	2	2	2
Mineralization, NOS	1	1	1	2	1	2	2	2	2	1
URINARY BLADDER	*	*	*	*	*	*	*	*	*	*
PROSTATE	*	*	*	*	*	*	*	*	*	*
STOMACH	*	*	*	*	*	*	*	*	*	*
DUODENUM	*	*	*	*	*	*	*	*	*	*
ILEUM	*	*	*	*	*	*	*	*	*	*
CECUM	*	*	*	*	*	*	*	*	*	*
RECTUM	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 90 Day DNB  
FATE: ALL  
DAYS ON TEST: ALL

STUDY NUMBER: 94-004  
GROUP: 7  
SEX: MALE

ANIMAL ID:	7-61	7-62	7-63	7-64	7-65	7-66	7-67	7-68	7-69	7-70
MESENTERIC LYMPH NODE	*	*	*	*	*	*	*	*	*	*
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIDES	*	*	*	*	*	*	*	*	*	*
SEMINAL VESICLE	*	*	*	*	*	*	*	*	*	*
SKIN	*	*	*	*	*	*	*	*	*	*
PREPUTIAL GLAND	*	*	*	*	*	*	*	*	*	*
EYES	*	*	*	*	*	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*	*	*	*	*	*
NASAL	*	*	*	*	*	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*	*	*	*	*	*

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 8

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	8-71	8-72	8-73	8-74	8-75	8-76	8-77	8-78	8-79	8-80
BRAIN	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N			N	N
Degeneration, Acinar	-	-	-	-	-	-	1	1	-	-
MANDIBULAR LYMPH NODE		N	N	N		N	N			N
Plasmacytosis	2	-	-	-	2	-	-	2	-	-
Hyperplasia, Lymphoid	-	-	-	-	-	-	-	-	2	-
ZYMBAL'S GLAND	N	N	N	N	N	U	N	N	N	N
PITUITARY	N	N	N	N	N	N	N	N	N	N
ADRENALS	N	N	N	N	N	N	N	N	N	N
THYROID	N	N	N	N	N	N	N	N	N	N
PARATHYROID	N	U	N	N	N	N	N	N	N	N
TRACHEA	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N		N	N	N	N		N
Hemorrhage	-	-	-	1	-	-	-	-	2	-

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)



Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 8

DAYS ON TEST: ALL

SEX: MALE

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ANIMAL ID:	8-71	8-72	8-73	8-74	8-75	8-76	8-77	8-78	8-79	8-80
HEART	N	N			N		N	N	N	
Inflammation, Chronic	-	-	1	1	-	1	-	-	-	1
COLON	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N		N	N	N	N		
Lymphocytic Infiltrates	-	-	-	-	-	-	-	-	1	-
Inflammation, Chronic	-	-	-	1	-	-	-	-	-	-
Hepatodiaphragmatic Nodule	-	-	-	-	-	-	-	-	-	P
SPLEEN	N	N		N	N	N	N	N	N	
Fibrosis	-	-	-	-	-	-	-	-	-	1
Hyperplasia, Lymphocytic	-	-	2	-	-	-	-	-	-	-
TONGUE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNGS	N	N		N					N	
Inflammation, Chronic	-	-	1	-	1	1	1	1	-	1
KIDNEY										
Regeneration, Tubular	2	1	1	2	1	1	2	1	2	1
Degeneration, Tubular	2	1	2	2	1	2	2	2	2	2
Mineralization, NOS	1	1	1	2	1	2	2	2	2	1
URINARY BLADDER		N	N	N	N	N	N	N		U
Urolith, NOS	P	-	-	-	-	-	-	-	P	-

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 94-004  
 90 Day 1,3-Dinitrobenzene  
 Exposure in Fischer 344 Rats

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TABULATED ANIMAL DATA

---

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 8

DAYS ON TEST: ALL

SEX: MALE

---

ANIMAL ID:	8-71	8-72	8-73	8-74	8-75	8-76	8-77	8-78	8-79	8-80
PROSTATE	N	N	N	N	N	N		N	N	U
Inflammation, Chronic/Active	-	-	-	-	-	-	2	-	-	-
STOMACH	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N			N	N	N
Inflammation, Chronic	-	-	-	-	-	-	2	-	-	-
Inflammation, Chronic/Active, Mesentery	-	-	-	-	-	2	-	-	-	-
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYIMIDES	N	N	N	N	N	N	N	N	N	N
SEMINAL VESICLE	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
PREPUTIAL GLAND							N		N	
Inflammation, Chronic/Active	-	-	3	-	-	2	-	2	-	2
Inflammation, Suppurative	-	-	-	3	-	-	-	-	-	-
Lymphocytic Infiltrates	1	2	2	2	1	2	-	1	-	2
EYES	N				N	N	N	N		
Microgranuloma, Cornea	-	2	2	1	-	-	-	-	1	2

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 8

DAYS ON TEST: ALL

SEX: MALE  
-----

ANIMAL ID:	8-71	8-72	8-73	8-74	8-75	8-76	8-77	8-78	8-79	8-80
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
FEMUR/STERNUM	N	N	N	N	N	N	N	N	N	N
NASAL	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

(END OF REPORT)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

---

CORRELATION OF GROSS & MICRO

---

STUDY ID : 90 Day DNB

STUDY NUMBER: 94-004

FATE: ALL

GROUP: 1

DAYS ON TEST: ALL

SEX: FEMALE

---

No Gross Observations for any animal in this group

---

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day DNB

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-004

GROUP: 2

SEX: FEMALE

Animal ID: 2-14

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

BRAIN - Discoloration, 2mm x 4mm, 1, Irregular, Brown

Related Histopathology:

BRAIN - Astrocytoma

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day DNB  
FATE: ALL  
DAYS ON TEST: ALL

STUDY NUMBER: 94-004  
GROUP: 3  
SEX: FEMALE

Animal ID: 3-25  
Animal Fate: Terminal Sacrifice

Pathologist: GRO  
Days on Test: 90

Reference to Necropsy Record:

OVARIES - Right, Discolored, 15x10x5 mm, 1, Irregular,  
Red/Tan, Periovary

Related Histopathology:

OVARIES - Necrosis, Parovarian; OVARIES - Inflammation,  
Chronic/Active, Parovarian

Animal ID: 3-29  
Animal Fate: Terminal Sacrifice

Pathologist: GRO  
Days on Test: 90

Reference to Necropsy Record:

OVARIES - Left, Cyst, 5x3x3 mm, 1, Round, Red

Related Histopathology:

OVARIES - Cyst, NOS

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day DNB

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-004

GROUP: 4

SEX: FEMALE

Animal ID: 4-34

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

OVARIES - Right, Cyst, 4x3x3 mm, 1, Round, Red

LIVER - Median, 5x6x1 mm, 1, Round, Tan

Related Histopathology:

OVARIES - Bursal Cyst

LIVER - Hepatodiaphragmatic Nodule

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

---

CORRELATION OF GROSS & MICRO

---

STUDY ID : 90 Day DNB

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-004

GROUP: 5

SEX: MALE

---

Animal ID: 5-41

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Decreased in Size, (Right)  
18x10x10 mm, (Left) 20x10x10 mm

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

---

Animal ID: 5-42

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Small, 16x9x9 mm, 2

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

---

Animal ID: 5-43

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Decreased in Size, (Left) 18x11x8  
mm, (Right) 10x17x7 mm

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

---

Animal ID: 5-44

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Small, 15x9x9 mm, 2

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

---

(REPORT CONTINUED)



Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

---

CORRELATION OF GROSS & MICRO

---

STUDY ID : 90 Day DNB

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-004

GROUP: 5

SEX: MALE

---

Animal ID: 5-45

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Decreased in Size, 15x8x9 mm, 2

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

---

Animal ID: 5-46

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Decreased in Size, (Left) 18x10x7  
mm, (Right) 17x10x8 mm

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

---

Animal ID: 5-47

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Decreased in Size, 11x8x9 mm, 2

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

---

Animal ID: 5-48

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Small, 13x7x7 mm, 2

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

---

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day DNB

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-004

GROUP: 5

SEX: MALE

Animal ID: 5-49

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Decreased in Size, 13x10x9 mm, 2

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

Animal ID: 5-50

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

TESTES - Bilateral, Decreased in Size, 14x9x8 mm, 2

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubule

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day DNB  
FATE: ALL  
DAYS ON TEST: ALL

STUDY NUMBER: 94-004  
GROUP: 6  
SEX: MALE

Animal ID: 6-59  
Animal Fate: Terminal Sacrifice

Pathologist: GRO  
Days on Test: 90

Reference to Necropsy Record:  
THYMUS - Discolored, Red

Related Histopathology:  
THYMUS - Hemorrhage

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day DNB

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-004

GROUP: 7

SEX: MALE

Animal ID: 7-66

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

THYMUS - Discolored, Red

Related Histopathology:

THYMUS - Hemorrhage

Animal ID: 7-69

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

THYMUS - Discolored, Red

Related Histopathology:

THYMUS - Hemorrhage

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 94-004  
90 Day 1,3-Dinitrobenzene  
Exposure in Fischer 344 Rats

---

CORRELATION OF GROSS & MICRO

---

STUDY ID : 90 Day DNB

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-004

GROUP: 8

SEX: MALE

---

Animal ID: 8-78

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

KIDNEY - Left, Discolored, 5x3 mm, 1, Irregular, Tan

Related Histopathology:

KIDNEY - Degeneration, Tubular

---

Animal ID: 8-79

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

THYMUS - Discolored, Red

Related Histopathology:

THYMUS - Hemorrhage

SEMINAL VESICLE - Decreased in Size, Moderate

SEMINAL VESICLE - No Corollary change detected

---

Animal ID: 8-80

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 90

Reference to Necropsy Record:

LIVER - Median Lobe, Nodule, 6x8x4 mm, 1, Irregular,  
Firm

Related Histopathology:

LIVER - Hepatodiaphragmatic Nodule

---

(END OF REPORT)



APPENDIX I  
CHEMICAL ANALYSES

Determination of Homogeneity  
of 1,3-Dinitrobenzene in the Diet

Target Diet Concentration (mg/kg)	Site of Sampling	Concentration by Analysis (mg/kg)	Mean Concentration (mg/kg)	Deviation from Mean (%)
WEEK 1				
30	Top	29.1	29.0	0.38
	Middle	28.8		0.60
	Bottom	29.0		0.22
6	Top	6.09	6.01	1.25
	Middle	5.93		1.44
	Bottom	6.02		0.18
1	Top	0.98	0.98	0.42
	Middle	0.91		6.70
	Bottom	1.04		6.28
WEEK 2				
30	Top	28.5	28.6	0.14
	Middle	28.7		0.31
	Bottom	28.5		0.17
6	Top	5.90	6.06	2.59
	Middle	6.46		6.63
	Bottom	5.82		4.05
1	Top	1.00	0.98	2.24
	Middle	0.91		6.90
	Bottom	1.03		4.66



Determination of Homogeneity  
of 1,3-Dinitrobenzene in the Diet

Target Diet Concentration (mg/kg)	Site of Sampling	Concentration by Analysis (mg/kg)	Mean Concentration (mg/kg)	Deviation from Mean (%)
WEEK 3				
30	Top	28.4	28.8	1.18
	Middle	28.2		2.14
	Bottom	29.7		3.33
6	Top	5.83	5.76	1.06
	Middle	5.85		1.48
	Bottom	5.62		2.54
1	Top	1.01	1.03	1.26
	Middle	1.05		2.25
	Bottom	1.02		0.99
WEEK 4				
30	Top	29.6	28.8	2.88
	Middle	28.6		0.71
	Bottom	28.2		2.17
6	Top	5.86	6.06	3.40
	Middle	6.09		0.39
	Bottom	6.25		3.01
1	Top	0.95	0.96	1.41
	Middle	0.93		3.65
	Bottom	1.01		5.05

Determination of Homogeneity  
of 1,3-Dinitrobenzene in the Diet

Target Diet Concentration (mg/kg)	Site of Sampling	Concentration by Analysis (mg/kg)	Mean Concentration (mg/kg)	Deviation from Mean (%)
WEEK 5				
30	Top	29.9	30.8	2.70
	Middle	31.2		1.30
	Bottom	31.2		1.41
6	Top	6.23	5.79	7.59
	Middle	5.56		4.05
	Bottom	5.59		3.54
1	Top	0.99	1.01	1.78
	Middle	1.00		0.47
	Bottom	1.03		2.24
WEEK 6				
30	Top	29.0	29.4	1.45
	Middle	29.8		1.40
	Bottom	29.5		0.05
6	Top	5.89	6.04	2.54
	Middle	6.09		0.74
	Bottom	6.15		1.81
1	Top	0.96	0.99	2.40
	Middle	0.99		0.70
	Bottom	1.00		1.70

Determination of Homogeneity  
of 1,3-Dinitrobenzene in the Diet

Target Diet Concentration (mg/kg)	Site of Sampling	Concentration by Analysis (mg/kg)	Mean Concentration (mg/kg)	Deviation from Mean (%)
WEEK 7				
30	Top	27.8	28.5	2.49
	Middle	29.3		2.54
	Bottom	28.5		0.05
6	Top	5.98	6.06	1.33
	Middle	6.29		3.87
	Bottom	5.90		2.54
1	Top	1.03	1.01	1.90
	Middle	0.98		2.63
	Bottom	1.01		0.73
WEEK 8				
30	Top	30.1	29.3	2.51
	Middle	29.7		1.27
	Bottom	28.2		3.78
6	Top	6.43	6.28	2.33
	Middle	6.20		1.30
	Bottom	6.22		1.03
1	Top	1.06	1.03	3.03
	Middle	0.97		5.61
	Bottom	1.06		2.58

Determination of Homogeneity  
of 1,3-Dinitrobenzene in the Diet

Target Diet Concentration (mg/kg)	Site of Sampling	Concentration by Analysis (mg/kg)	Mean Concentration (mg/kg)	Deviation from Mean (%)
WEEK 9				
30	Top	29.0	29.5	1.81
	Middle	27.7		6.12
	Bottom	31.8		7.93
6	Top	6.37	6.10	4.42
	Middle	5.79		5.18
	Bottom	6.15		0.76
1	Top	1.04	1.01	2.46
	Middle	1.03		1.33
	Bottom	0.98		3.79
WEEK 10				
30	Top	29.4	30.5	3.54
	Middle	32.1		5.00
	Bottom	30.1		1.47
6	Top	6.35	6.06	4.80
	Middle	5.51		9.05
	Bottom	6.32		4.26
1	Top	1.02	1.03	0.87
	Middle	0.99		4.32
	Bottom	1.08		5.19

Determination of Homogeneity  
of 1,3-Dinitrobenzene in the Diet

Target Diet Concentration (mg/kg)	Site of Sampling	Concentration by Analysis (mg/kg)	Mean Concentration (mg/kg)	Deviation from Mean (%)
WEEK 11				
30	Top	29.7	29.2	1.73
	Middle	29.0		0.43
	Bottom	28.8		1.30
6	Top	6.07	5.83	4.25
	Middle	5.74		1.52
	Bottom	5.67		2.74
1	Top	0.95	0.99	4.20
	Middle	1.06		7.08
	Bottom	0.96		2.88
WEEK 12				
30	Top	30.0	30.6	1.95
	Middle	31.8		3.84
	Bottom	30.0		1.89
6	Top	5.57	5.71	2.46
	Middle	5.76		0.86
	Bottom	5.80		1.59
1	Top	1.02	1.01	1.88
	Middle	0.97		3.18
	Bottom	1.02		1.30

Determination of Homogeneity  
of 1,3-Dinitrobenzene in the Diet

Target Diet Concentration (mg/kg)	Site of Sampling	Concentration by Analysis (mg/kg)	Mean Concentration (mg/kg)	Deviation from Mean (%)
WEEK 13				
30	Top	30.4	30.4	0.03
	Middle	30.1		1.00
	Bottom	30.7		1.03
6	Top	5.78	5.97	3.25
	Middle	5.69		4.79
	Bottom	6.45		8.04
1	Top	1.03	1.04	0.69
	Middle	1.03		1.17
	Bottom	1.06		1.86

Analysis of Feed Mixtures  
of 1,3-Dinitrobenzene

Target Diet Concentration (mg/kg)	Date Prepared	Date Analyzed	Concentration by Analysis (mg/kg)	% Error
Week 1				
30	19 Aug 94	23 Aug 94	29.0	3.40
6	17 Aug 94	22 Aug 94	6.01	0.22
1	15 Aug 94	23 Aug 94	0.98	2.04
Week 2				
30	26 Aug 94	6 Sep 94	28.6	4.77
6	24 Aug 94	2 Sep 94	6.06	1.00
1	22 Aug 94	6 Sep 94	0.98	1.87
Week 3				
30	2 Sep 94	8 Sep 94	28.8	4.06
6	31 Aug 94	8 Sep 94	5.76	3.94
1	29 Aug 94	8 Sep 94	1.03	2.53
Week 4				
30	9 Sep 94	19 Sep 94	28.8	3.94
6	7 Sep 94	21 Sep 94	6.06	1.06
1	8 Sep 94	21 Sep 94	0.96	3.99
Week 5				
30	16 Sep 94	27 Sep 94	30.8	2.57
6	14 Sep 94	23 Sep 94	5.79	3.48
1	12 Sep 94	23 Sep 94	1.01	0.89

Analysis of Feed Mixtures  
of 1,3-Dinitrobenzene

Target Diet Concentration (mg/kg)	Date Prepared	Date Analyzed	Concentration by Analysis (mg/kg)	% Error
Week 6				
30	20 Sep 94	3 Oct 94	29.4	1.88
6	19 Sep 94	3 Oct 94	6.04	0.71
1	16 Sep 94	4 Oct 94	0.99	1.20
Week 7				
30	26 Sep 94	6 Oct 94	28.5	4.89
6	28 Sep 94	4 Oct 94	6.06	0.95
1	30 Sep 94	5 Oct 94	1.01	0.69
Week 8				
30	7 Oct 94	13 Oct 94	29.3	2.19
6	7 Oct 94	13 Oct 94	6.28	4.73
1	3 Oct 94	13 Oct 94	1.03	3.05
Week 9				
30	11 Oct 94	19 Oct 94	29.5	1.68
6	11 Oct 94	19 Oct 94	6.10	1.73
1	12 Oct 94	17 Oct 94	1.01	1.36
Week 10				
30	20 Oct 94	25 Oct 94	30.5	1.76
6	20 Oct 94	26 Oct 94	6.06	1.05
1	20 Oct 94	26 Oct 94	1.03	2.97



Analysis of Feed Mixtures  
of 1,3-Dinitrobenzene

Target Diet Concentration (mg/kg)	Date Prepared	Date Analyzed	Concentration by Analysis (mg/kg)	% Error
Week 11				
30	24 Oct 94	2 Nov 94	29.2	2.77
6	24 Oct 94	2 Nov 94	5.83	2.89
1	24 Oct 94	3 Nov 94	0.99	0.84
Week 12				
30	31 Oct 94	9 Nov 94	30.6	2.09
6	31 Oct 94	9 Nov 94	5.71	4.87
1	31 Oct 94	8 Nov 94	1.01	0.59
Week 13				
30	9 Nov 94	16 Nov 94	30.4	1.28
6	10 Nov 94	16 Nov 94	5.97	0.48
1	10 Nov 94	16 Nov 94	1.04	3.78

APPENDIX J  
PROTOCOL AND  
AMENDMENTS

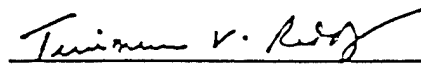
## PROTOCOL

### 90 Day Subchronic Toxicity Evaluation of 1,3-Dinitrobenzene (DNB) in Fischer (F344) Rats

This study will be conducted in agreement with Good Laboratory Practice Standards, Environmental Protection Agency, Toxic Substances Control Act (TSCA) 40 CFR Part 792 (Federal Register, Vol 54, No. 158, August 17, 1989, pp. 34034 - 34050). All aspects of the studies will be conducted in accordance with written Standard Operating Procedures (SOP) of the performing unit and all raw data and performance documents will be maintained in agreement with GLP. An administratively separate quality assurance unit (QAU from PAI) will monitor the studies to assure adherence to good laboratory practices and the approved SOPs. Any deviation from the protocol or GLP will be noted in the raw data and reflected in the final report.

Testing Facility  
A.W. Breidenbach Environmental Research Center  
U.S. Environmental Protection Agency  
Cincinnati, OH 45268

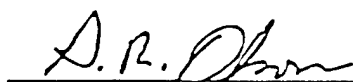
Prime Contractor (Sponsor)  
U.S. Army Biomedical Research and  
Development Laboratory, Fort Detrick  
Frederick, Maryland 21701-5010

  
Principal Investigator  
T.V. Reddy, Ph.D.

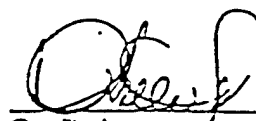
8-16-94  
Date

  
G. Reddy, Ph.D., Sponsor

8-22-94  
Date

  
Project Manager  
G.R. Olson, DVM, Ph.D.  
Pathology Associates, Inc.

8-16-94  
Date

  
Quality Assurance  
W.R. Fox, MA  
Pathology Associates, Inc.

8-16-94  
Date

90-DAY SUBCHRONIC TOXICITY EVALUATION OF  
1,3-DINITROBENZENE (DNB) IN FISCHER (F344) RATS

RESEARCH PROTOCOL

Tirumuru V. Reddy, Ph.D.  
Principal Investigator

F. Bernard Daniel, Ph.D.  
Co-Principal Investigator

Ecological Monitoring Research Division  
Environmental Monitoring Systems Laboratory  
U.S. Environmental Protection Agency  
Cincinnati, Ohio 45268

August 16, 1994

**TITLE:****90 DAY SUBCHRONIC TOXICITY EVALUATION OF  
1,3-DINITROBENZENE (DNB) IN FISCHER RATS**

**BACKGROUND:** Nitroaromatics, such as 1,3-dinitrobenzene (DNB), 1,3,5-trinitrobenzene (TNB), and N-methyl-N,2,4,6-tetranitroaniline (tetryl), have been detected as environmental contaminants of groundwater and soil near production sites and in some instances at military test grounds. The wastewaters discharged from trinitrotoluene (TNT) manufacturing processes contain a variety of aromatic compounds, including DNB and TNB. TNB is formed during the nitration step of TNT synthesis as a result of oxidation of methyl groups. Although the complete mechanism of TNB formation during TNT photolysis is unknown, Burlinson (1980) suggested that it is produced by decarboxylation of 2,4,6-trinitrobenzaldehyde, a major TNT photoproduct. It is also found in aquatic systems and surface soils as a by-products of photolysis of TNT. DNB and TNB are not easily biodegradable, persist in the environment, eventually leach out, and contaminate groundwater near waste disposal sites. Tetryl is an explosive that has been in use, largely for military purposes, since 1906. Wastewaters and soil at the original production sites and other plants devoted to munitions assembly, contain large quantities of tetryl. A recent estimate of tetryl in wastewaters generated from the production of tetryl at Joliet Army Ammunition Plant was about 36 lb/day of each production line.

Toxicity data on these compounds are limited. The oral LD50 of DNB, TNB and tetryl were 59 mg/kg, 284 mg/kg and greater than 5 g/kg, respectively, in rats for combined sexes. TNB and tetryl were not toxic at 2 g/kg when applied to rabbit skin for 24 hours. However, the dermal LD50 of DNB was 1.99 g/kg for combined sexes of rabbits. None of these compounds produced skin irritation potentials but positive (DNB) and severe (TNB, tetryl) eye irritation potentials in rabbits. The sensitization tests showed that DNB and tetryl are not skin sensitizers while TNB caused mild allergic reaction in guinea pigs. Some of the toxicological and behavioral effects of DNB are; formation of methemoglobin, testicular degeneration and reproductive failure, and weight loss and anemia in hamsters, rats and mice. Neurological and hematological disorders have also been reported in dogs. DNB is rather toxic to humans; the estimated lethal dose range is 5-50 mg/kg. It is readily absorbed through the skin. Fetal doses (amount and route of administration are not given) of tetryl produced toxic degeneration (necrosis) in the kidneys of dogs and rabbits and liver necrosis in dogs (not in rabbits). Tetryl was observed to be a powerful skin sensitizer in ammunition plant workers. Hardy and Maloof (1950) reported effects from accidental exposure of 11 people to tetryl: two died, one was disabled and eight did not detect permanent disability. They also reported irreversible liver damage, dermatitis, and upper respiratory irritation following tetryl exposure. The effects of tetryl exposure include gastrointestinal symptoms and epidermal, respiratory, nervous system, hematopoietic and circulatory injury. Atmospheric concentration of 1.5 mg/m<sup>3</sup> or below did not produce systemic poisoning in persons working with tetryl. DNB, TNB, and tetryl have been shown to be genotoxic in *Salmonella* mutagenesis assay. TNB has been shown to form adducts of blood proteins and tissue DNA in rats.

## PROTOCOL

1. Study: 90-day Subchronic toxicity evaluation of DNB in F344 male and female rats. Starting date August 22 and 23, 1994 and the termination on November 22 and 23, 1994.
2. Purpose: To evaluate subchronic toxicity of DNB when administered in the diet for 90-days.
3. Study Location: Andrew W. Breidenbach Environmental Research Center, U.S. Environmental Protection Agency, Cincinnati, OH 45268
4. Sponsor and Address: U.S. Army Biomedical Research and Development Laboratory, Fort Detrick, Frederick, Maryland 21701-5010
5. Principal Investigator: T.V. Reddy, Ph.D., Research Chemist Environmental Monitoring Systems Laboratory, U.S. Environmental Protection Agency, Cincinnati, Ohio 45268
6. Co-Principal Investigator: F. Bernard Daniel, Ph.D, Environmental Monitoring Systems Laboratory, U.S. Environmental Protection Agency, Cincinnati, Ohio 45268
7. Study Coordinator: Barry Wiechman, MS., Pathology Associates (PAJ)
8. Project Manager: G.R. Olson, DVM, Ph.D., Pathology Associates (PAJ)
9. Regulatory Compliance: This study is carried out according to U.S. EPA Health Effects testing guidelines (40 CFR 798) in compliance with GLP (40 CFR 792)
10. Quality Assurance: The protocol in life phase and final report will be audited by the Quality Assurance Office in accordance with SOP's at Pathology Associates, West Chester, Ohio 45069.
11. Test Material: 1,3-Dinitrobenzene(DNB). Powder, (CAS#99-65-0), purchased from Fluka, USA and purity is more than 99%. The purity was further confirmed by HPLC.
12. Experimental Design:
  - A. Selection of Dose: Toxicon Corporation(Woburn, MA 01801)has conducted acute toxicity studies on DNB. They administered DNB in corn oil to rats at a single oral dose and observed the clinical signs for 14 days following dosing. Based on the results they have established that 59 mg/kg BW, as the LD50 dose for combined sexes. Based on the results from the 14 day range finding experiment. the following three dose levels; 30,

6, 1 mg 1,3-DNB/kg diet were selected for the 90 day subchronic toxicity study. Control rats are fed only powdered chow diet 5002. There are no known contaminants in the food that would affect the outcome of the study.

**B. Preparation of the Diet:** Certified powdered Purina laboratory chow purchased from Purina labs and stored at 4°C will be used. DNB diets are prepared once a week. Just before the diet preparation, DNB is removed from the storage shelves (kept in designated carcinogen room), weighed in the carcinogen room and mixed with the powdered diet (30 mg/kg diet). First, 30 mg DNB will be added to 250g powdered diet and mixed for 15 min. Then an additional 250 g of powdered diet is added and mixed for an additional 15 min. Then the remaining diet will be added to bring the DNB concentration to 30 mg/kg; then mixed for an additional hour in a mechanical stirrer (Kitchen Aid Model No. K5SS) for uniform distribution of DNB in the diet. This is also verified by determining the DNB concentration in the diet taken from three different depths (top, middle and bottom layer) of the mixing chamber. Quantitative analysis of DNB is done by HPLC.

The premixed diet (30 mg/kg) is further diluted with fresh powdered diet (0, 5 and 30 times) to obtain the desired DNB concentration. Individual diet concentrations are determined as described before. The diet feeders are refilled twice a week and changed weekly. DNB concentrations are manipulated in such a way that each rat (caged individually) will receive the desired amount of DNB. This is determined by calculating the daily average intake, followed by an adjustment of DNB content in the diet. Dietary intake and water consumption are measured twice a week. Body weights are recorded once a week.

**C. Animals:** 65 male and 65 female F344 rats (6 week old) with body weight range (110-125  $\pm$  5g) will be purchased and held for 2 weeks for quarantine. Male and female rats, after quarantine, are housed individually in clear polycarbonate shoe boxes in drawer rack cages with aspen bedding (San I Chips supplied by P.J. Murphy, Forest Products Corporation, NJ). Shoe boxes and bedding are changed along with food and water (2 times a week). Water is provided with 16 ounce bottles and stoppers with sippers tubes. There are no known contaminants in the water that would affect the outcome of the study. At all times the animal rooms are maintained on a 12 hour light/dark cycle at 22-23 C with a relative humidity range of 40-60%. All rats are identified by electronic implants.

**D. Randomization:** Using computer-generated random numbers with assignment to groups. At the time of randomization, the weight variation of the animals of each sex used should not exceed  $\pm 2 S \pm D$  of the mean weight, and the mean body weights for each group of each sex will not be statistically different.

**E. Justification:** Rats historically have been used in safety evaluation studies and are recommended by appropriate regulatory agencies.

G. Group designation and dose levels for 90-day toxicity study.

Group	No. of Rats	Sex	mg DNB/kg diet	Sacrifice Time (days)
1	15	Male	30	90
2	15	"	6	90
3	15	"	1	90
4	15	"	0	90
5	15	Female	30	90
6	15	"	6	90
7	15	"	1	90
8	15	"	0	90

\* Five rats from each group (1-8) will be sacrificed after 45 days for hematology and clinical chemistry. The remaining 10 rats are sacrificed after 90 days of DNB exposure.

H. Analysis of the Diet: The homogeneity of DNB in the diet is determined by analyzing the DNB content (by HPLC) in the diet, soon after diet preparation.

I. Observation of Animals:

(1) Clinical Observations:

Twice daily - mortality and morbidity check.

Once daily - cageside observation for obvious indications of a toxic effect; these effects will be recorded as they are observed.

Data for mortality and morbidity checks and cageside observations will be recorded on the same form. Because these are cageside animal checks, the observations will not be as specific and may not necessarily duplicate those observations recorded on body weight days when thorough physical examinations are conducted.

(2) Physical Examinations: At each weighing interval - These observations will include, but not be limited to, changes in: skin and fur; eyes and mucous membranes; respiratory, circulatory, autonomic and central nervous systems; some motor activity and behavior.

(3) Body Weight: Prior to treatment and weekly, thereafter.



- (4) Food Consumption: Twice weekly
- (5) Water Consumption: Twice weekly
- (6) Ophthalmoscopic examination: Prior to the treatment and at termination by a board certified opthamologist

#### J. Clinical pathology

- (1) Frequency: 45 days and 90 days.
- (2) Number of Animals: five animals per group at 45 days and 10 animals per group at 90 days.

#### K. Tests:

##### (1) Hematology:

leukocyte count	methemoglobin
erythrocyte count	hematocrit
heinz bodies	platelet count
hemoglobin	differential leukocyte count

##### (2) Blood Chemistry:

glucose	urea nitrogen
sodium	creatinine
potassium	
total protein	aspartate aminotransferase
phosphorus	alkaline phosphatase
albumin	alanine aminotransferase
calcium	cholesterol
total bilirubin	triglycerides

#### L. Termination:

- (1) Unscheduled Sacrifices and Deaths: Necropsies by trained personnel using procedures approved by board-certified pathologists will be conducted on all moribund animals and on all animals that die.
- (2) Sacrifice: After 90 days of treatment, all surviving animals will be weighed, anesthetized with sodium pentobarbital, and exsanguinated. Necropsies will be conducted on each animal in a random order to eliminate bias. Animals will be fasted for 12 hrs before sacrifice. A pathologist will be readily available for consultation (further participation by a pathologist is available).

## M. Postmortem Procedures:

### (1) Gross Necropsy:

The necropsy will include examination of:

External surfaces

All orifices

Cranial cavity

Carcass

External surface of the brain (at necropsy) - cut surfaces of the brain

The thoracic, abdominal and pelvic cavities and their viscera

The cervical tissues and organs

### (2) Organ Weights:

For each terminally sacrificed animal, the following organs will be weighed following careful dissection and trimming to remove fat and other contiguous tissue in a uniform manner:

brain	lungs
liver	thymus
spleen	testes with epididymides/ovaries
kidneys	heart
adrenals	

### (3) Tissue Preservation: The following tissues (when present) from each animal will be preserved in 10% neutral buffered formalin:

skin	ileum
mandibular lymph nodes	colon
mesenteric lymph nodes	cecum
mammary glands	rectum
thigh muscle	liver
sciatic nerve	pancreas
sternum with marrow	spleen
femur with marrow	kidneys
larynx	adrenals
thymus	urinary bladder
trachea	seminal vesicles
lungs and bronchi	prostate
heart and aorta	testes, including epididymis
thyroid	ovaries
parathyroids	uterus

esophagus  
 stomach  
 duodenum  
 jejunum  
 tongue  
 salivary gland

nasal cavity/ turbinates  
 brain  
 pituitary  
 preputial or clitoral glands  
 Zymbal's gland  
 thoracic spinal cord

#### N. Histopathology:

(1) Following necropsy, a list of all gross lesions recorded will be submitted to the project officer at U.S. Army Biomedical Research and Development Laboratory for his evaluation and for any additional histopathology other than those described below.

Histopathological evaluations are to be done on the following tissues from all the animals (male and female from the highest dose group and untreated controls). The tissues examined under a light microscope are as follows:

cerebrum  
 cerebellum  
 trachea  
 thyroid  
 parathyroid  
 esophagus  
 salivary gland  
 harderian gland  
 heart  
 aorta  
 lung  
 thymus  
 spleen  
 mesenteric lymph node  
 liver  
 kidneys  
 urinary bladder  
 duodenum  
 jejunum  
 ileum

pancreas  
 cecum  
 colon  
 rectum  
 stomach  
 skeletal muscle  
 sciatic nerve  
 tongue  
 skin  
 mammary gland  
 nasal region  
 sternum  
 femur  
  
 spinal cord  
 adrenals  
 pituitary  
 eye(s)  
 zymbal's gland

#### MALE

accessory sex glands  
 epididymis  
 testes

#### FEMALE

uterus  
 ovaries

An average of 12 slides will be prepared for each rat covering all the tissues shown above (3 or 4 tissues are fixed on each slide). A total of 480 slides from 40 rats from the 90-day study will be examined. Based on the results from high dose group tissues, examination of tissues from other dose groups will be conducted as needed. Following completion of each study, all wet tissues, paraffin blocks and slides will be placed in the EPA archives.

#### O. Final Report:

Four months after the termination of the in-life phase of the study, 8 copies of the final report which includes the following information (as appropriate) will be prepared and submitted to the project officer at EPA:

- (1) Experimental Design and Methods:
- (2) Results:

mortality	organ weights and organ/body
clinical observations	weight ratios
body weights	gross pathology
food and liquid consumption	histopathology
clinical pathology tests	

#### Statistical Evaluation:

Dunnet's t-test will be used for comparing the treatment groups. Kruskal-Wallis rank sums will be used, if needed, to examine the differences among the treatment groups and Wilcoxon rank sum test will be used to analyze pairwise differences between the control and each dose group.

Deviations from GLP's and Protocol

1. Diet preparation as stated in the narrative of this report was adapted in order to better utilize technician time.

Tirumuru V. Reddy

Tirumuru V. Reddy, Ph.D.

7-31-95

Date

## DISTRIBUTION LIST

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